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PARTIAL GASTRECTOMY AND PEPTIC ULCER

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Peptic ulcer appears to have been a rare condition before the twentieth century. Duodenal ulcer in particular seems to have developed with the rush and hurry of modern civilization. As the decades have succeeded one another the disease has increased in frequency and apparently also in severity. Conservative measures have failed to control an increasing number of cases, and surgical intervention is required more often in treatment. Moreover, the relatively simple operation of gastro-enterostomy, which appeared adequate to control the disease in former years, seems now to fail before the pressure of stomal ulceration.

Partial gastrectomy has become the standard operation, but the best design of this operation has never been agreed. Large or small stomata, placed in front of or behind the colon, with or without valves, directed to right or to left, are employed in various combinations, and the view has gained ground that the design of partial gastrectomy is not a matter of importance. Nevertheless the incidence of post-gastrectomy syndromes varies enormously. Some centres report their researches into the problems of burst duodenal stumps and bile vomiting. Other surgeons read these papers with silent wonder at why they do not have the same experience.

This paper is an attempt to correlate the frequency and severity of post-gastrectomy syndromes with the technique used in the operation. A method of gastrectomy is described which is not followed by serious post-operative symptoms. The inadequacy of gastro-enterostomy must, however, first be illustrated.

Gastro-enterostomy and Duodenal Ulcer

The object of this operation is to prevent any accumulation of acid juice in the stomach as the result of hypersecretion and pylorospasm. The effect is to heal the duodenal ulcer, and the operation can be relied upon to do so. Symptoms of post-gastrectomy type are extremely rare after gastro-enterostomy. In a recent review D. H. Clark (1958, personal communication) found only two examples of "dumping" in 300 cases, and A. W. Kay (1958, personal communication) had only one such case in 150 patients. I have no examples in 125 cases of my own.

The great advantage of gastro-enterostomy is that the patient retains his stomach and with it his full gastronomic ability. He can eat and drink a full meal and get on with his work. His stomach does not empty as precipitately as it does after partial gastrectomy, and indeed some of the food continues to be carried by antral peristalsis via the duodenum. Apart from the safety valve provided by the stoma, the stomach behaves physiologically and the patient returns to his normal health and vigour.

The operation is excellent in every respect but one—the vulnerability of the stoma to further ulceration. In the early part of the century this was put at less than 4%, but later Clark (1951), in a careful follow-through study found that the results were poor in one-third of the cases, with a "hard core" of 18% of serious gastrojejunal ulcers. My own results are indicated in Table I, which refers to a group of 51 duodenal ulcer patients subjected to gastro-enterostomy more than 15 years ago. For simplicity the results are expressed as percentages, corrected to allow for five deaths from unassociated causes and for three patients with whom contact was lost halfway through the follow-up period. Those patients described as "fully well" possess a robust digestive system that few cases of partial gastrectomy can claim. The term "slight relapse" denotes patients with rare episodes of mild discomfort. They are well satisfied with the operation and regard themselves as cured.

TABLE I.—*Results of Gastro-enterostomy for Duodenal Ulcer*

Time since Operation	Good Result (%)			Recurrent Ulcer (%)
	Fully Well	Slight Relapse	Total	
Up to 4 years ..	86	6	92	8
At 5 years ..	72	12	84	16
,, 10 ,, ..	56	15	71	29
15–18 ,, ..	45	17	62	38

It will be seen that 15 years after gastro-enterostomy not quite one-half of my patients are fully well: nearly two-thirds may fairly be regarded as satisfactory. By that time, however, over one-third of all patients have developed a stomal ulcer. Table I indicates that the stoma continues to be vulnerable over the years and that the recurrent ulceration is not confined to the early post-operative period. Most of the patients with gastro-jejunal ulcer were treated by partial gastrectomy and have had no recurrence of symptoms since. Three, however, died from an acute complication of the stomal ulcer before gastrectomy was decided upon.

These results are very similar to those of Clark, and it is probable that the ultimate incidence of gastrojejunal ulcer after gastro-enterostomy for duodenal ulcer is of the order of 38%. It may be debated whether the difference between these results and the earlier recorded figures is real or apparent. Follow-through departments with

statistical discipline and regularized attendance were infrequent in the early days, while methods of investigation were not so searching as they are now. Gastroscopy did not exist, radiological methods were less detailed, and a loose conception of "gastritis" was used to describe cases of dyspepsia with negative findings. The early published figures may therefore not be comparable with modern ones.

In 1918 Walton had established a follow-through department at the London Hospital. From then onwards he personally interviewed his old patients at a regular weekly clinic, at which it was later my privilege to assist. In 1934 he reported a 3.2% incidence of gastrojejunal ulcer in a large series of cases (Walton, 1934). This figure was the number of cases recognized by *x*-ray examination or by surgical exploration. It did not include the undiagnosed dyspeptics whom the advent of gastroscopy was later to reveal as stomal ulcer cases also. It is probable, therefore, that Walton's recorded incidence of gastrojejunal ulcer was less than the real figure. This correction, however, is certainly not of such a degree as to explain the tenfold difference between his figures and those in Table I. It seems probable that the increasing vulnerability of the stoma after gastro-enterostomy is real and, like duodenal ulcer itself, is an example of the increasing intensity of the peptic ulcer phenomenon in the modern community.

Effect of Time on Results of Surgery: Vagotomy

Table I illustrates another matter of more general significance. It portrays the results of simple gastro-enterostomy as they appeared at different stages of follow-through observation. The figures that were so gratifying up to four years after operation did not look so well 10 years later. The moral of this should be borne in mind when considering the various "new" operations on the stomach which are being performed for peptic ulcer. The addition of vagotomy to gastro-enterostomy is the most promising of these. It is, however, still a new procedure, and the results should be viewed with some reserve until enough time has elapsed to allow a mature judgment to be made. Clearly, the results of gastro-enterostomy alone are not good enough.

Gastric Ulcer and the Billroth I Gastrectomy

So far the discussion has been limited to the problems of hyperacidity and stomal ulceration after gastro-enterostomy. These are the concern of duodenal ulcer cases. There is, however, little hypersecretion in association with gastric ulcer, and problems of anastomotic ulcer after operation do not arise.

For gastric ulcer the sole object is the removal of the lesion: an extensive resection is not required, and a Billroth I anastomosis is easily arranged. With this operation the gastro-duodeno-jejunal sequence in the onward passage of food is preserved and bile can mix freely with it. There is consequently a minimum of interference with digestion and nutrition. Simple dumping symptoms may occur, but since there is no element of obstruction they are easily controlled and the results are excellent (see Table III).

Duodenal Ulcer and the Polya Gastrectomy

Unfortunately the Billroth I operation will not do for duodenal ulcer because, like gastro-enterostomy, stomal ulceration develops in a high proportion of cases. Thus Goligher, Moir, and Wrigley (1956) found 17% of cases developed a gastroduodenal ulcer. They suggested that the explanation was the movement of alkaline juice away from the Billroth stoma, which was thereby exposed to the acid secretion of the remnant of the stomach. In a Polya type gastrectomy the movement of alkaline juice is towards the jejunal stoma, which is thereby protected from recurrent ulceration. For duodenal ulcer, therefore, a Polya gastrectomy must be performed, but to achieve security at least three-quarters of the stomach must be removed (Wells and MacPhee, 1954).

The price to be paid is a subsequent lack of full strength and vigour and a group of effects which have been called the post-gastrectomy syndrome. The term is unfortunate, because a number of symptoms due to faulty anastomoses have been lumped together with the effects necessarily due to the loss of the stomach. The latter—for example, a tendency to anaemia due to deficient absorption of iron—are generally amenable to treatment. The more serious symptoms, such as bile vomiting, are due to intestinal obstruction at the stoma. They are not due to the loss of the stomach and should not be included as part of any syndrome. The phenomenon of "dumping" therefore needs close examination.

Dumping

Dumping is a condition which follows the too-rapid emptying of the stomach into the jejunum. It is due not so much to the reduced capacity of the stomach as to the loss of the regulating mechanism of the pylorus. In the intact stomach this mechanism can be observed by cineradiography after a barium meal. The pyloric mill takes the ingested food portion by portion, mixes it to and fro with a little regurgitant duodenal juice, and passes it through the sphincter. In the duodenum it moves forwards and backwards again, taking up its admixture of bile and pancreatic juice until it is delivered by a peristaltic wave into the jejunum. In this way each bolus of food is adjusted in size, dilution, *p*H, and content of enzymes before it is allowed to pass on, and the jejunum is protected from all chemical and mechanical assaults.

After a partial gastrectomy this protection is completely lost, and after a meal the food is "dumped" unchanged into the jejunum in the space of a few minutes. The inrush of the meal excites sympathetic reflexes from the gut resulting in symptoms of fullness and discomfort locally, together with more generalized effects such as weakness, faintness, tachycardia, and sweating. These manifestations comprise the dumping syndrome, which is a crude but not unsatisfactory description, provided it is realized that both the abdominal and the general symptoms are different aspects of the same reflex. There is nothing to be gained by an attempt to restrict the term only to the general group.

It is important to recognize that there is no element of obstruction in dumping. The symptoms are due solely to the invasion of the unprotected jejunum by food. They can therefore be avoided by reducing the rate of outflow from the gastric remnant to the level at which it can be accepted without distress by the jejunum. The patient can do this by eating slowly, avoiding liquid foods, and deferring drinks until the first wave of food has passed on. Hypertonic solutions seem to exert a powerful stimulus to the jejunum, and

so sweet articles of diet should be avoided at a main meal. Fortunately essential protein foods like meat are relatively inert and can be taken in quantity, and a moderate intake of fat is innocuous. The meal-time restrictions of the gastrectomized patient are therefore not too onerous provided that all he has to deal with are the simple uncomplicated dumping effects just described.

Bile Vomiting

Bile vomiting is *not* a part of the dumping phenomenon. It is due to intestinal obstruction at the stoma and dilatation of the afferent loop of jejunum with bile, until a peristaltic heave empties it into the stomach. The point of obstruction lies at the junction of the afferent jejunum and the lesser-curve end of the gastric stump (Fig. 1). A kink is apt to form here at the end of the gastrectomy operation when the stump of the stomach is allowed to fall back to its position under the diaphragm, drawing the anastomosis up with it. Thereafter bile tends to collect behind the kink and the symptoms which follow depend on the degree of obstruction caused by it.

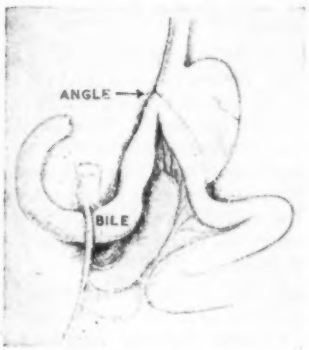

FIG. 1.—Afferent-loop obstruction caused by hitching jejunum to lesser curve.

In most cases the vomiting of bile begins soon after the operation. As the obstructed intestine hypertrophies it may diminish or cease altogether, leaving, however, a persistent sense of nausea. Some patients bring up a little bile every day. Others collect it in the afferent loop with increasing distress until relief comes from the vomiting of a large quantity of stale fluid. Loss of the biliary component in the digestion of fat may result in diarrhoea, steatorrhoea, and malnutrition. The chief symptoms, however, are the reflex effects of distension of the afferent jejunal loop by the bile, which are almost indistinguishable from the symptoms of dumping just described.

This similarity in the symptoms of dumping and of stomal obstruction is due to the fact that sympathetic afferent impulses from the whole of the jejunum are transmitted through one segment only, the ninth dorsal. A stimulus applied to one part of the jejunum therefore produces the same effects as a stimulus at any other part. Experimentally this may be a weighted bag, a distending balloon, or hypertonic solutions. Pathologically it may be a collection of obstructed bile in the afferent loop or a heavy meal dumped into the efferent loop. The reflex effects are all the same. The only difference is in their degree, which is much greater with the obstructive dilatation of the afferent loop than with the simple overloading of the efferent loop in true dumping.

Subemetic Afferent-Loop Obstruction. — It is important to recognize that lesser degrees of stomal obstruction can exist without the outward and visible sign of bile vomiting. This condition would then be indistinguishable from efferent-loop dumping except for one thing: true dumping symptoms can be controlled by the patient. He has only to exercise discrimination in his eating habits to reduce the symptoms to a tolerable level or to avoid them altogether. The victim of the afferent-loop syndrome cannot do this. No matter how careful he is, his jejunal loop is choked with bile and he cannot escape. If he is fortunate he may find that by lying down in a particular attitude the bile may leak into his stomach and pass on or be vomited. He may even prefer to eat his meals lying down. But he is afraid to eat. The summation of reflexes from food in the efferent jejunum and from an extra flow of bile into the afferent jejunum may result in complete prostration. Malnutrition and vitamin deficiencies now bring their own troubles, and the patient's misery is sealed by being classed as an intractable dumper.

Diagnosis and Treatment

Bile vomiting is pathognomonic of obstruction. Even minor and rare episodes of it are sure pointers to the diagnosis. With obstruction of the afferent loop the vomitus is a clear yellow fluid devoid of any food particles. Admixture of food with the bile indicates an obstruction in the efferent jejunum or beyond. Barium-meal examination will demonstrate at once the relatively uncommon distal stomal obstruction. In the radiology of afferent-loop obstruction the significant point is the failure of the meal to enter the proximal jejunum although the efferent jejunum appears quite normal.

In the absence of bile vomiting diagnosis must rest firmly on the basis that symptoms which fail to respond to simple eating rules are due to mechanical obstruction. The conception of intractable dumping must be firmly rejected.

Surgical exploration should be advised in all cases where symptoms are severe enough to justify it. At operation the parts will probably appear perfectly normal. The afferent loop may be bulky and hypertrophied, but it is unlikely to be found actually distended. The offending kink at the attachment of the jejunum to the lesser curve of the gastric stump may be obscured by filmy adhesions or by the mesocolon if the anastomosis was retrocolic. The surgeon must not be misled by these innocent appearances. The anastomosis must be dissected completely bare for inspection. Thoughtful manipulation of the parts may be needed to indicate the mechanics of the obstruction. Filling the afferent jejunum with saline by means of an oesophageal catheter negotiated into it may help to display the kink, especially if the stomach is drawn upon to exaggerate its acuteness and simulate the effect of the erect posture.

The obstruction can be relieved in several ways. The simplest is to anastomose the afferent and efferent loops together, without much dissection. Wells has used a "pantaloons" form of enteroplasty at the stoma with the same object in view. More recently Wells and Johnston (1956) have reported good results from conversion of the anastomosis to a Roux Y form. Yet another method is to undo the anastomosis entirely and make a Billroth I connexion with the old duodenal stump.

All these methods, however, divert the alkaline juices away from the stoma, and if the original lesion was a duodenal ulcer the conversion involves the risk of subsequent anastomotic ulceration. I therefore prefer to release the obstructing kink by detaching the jejunum from the lesser-curve half of the existing

anastomosis, retaining the greater-curve half as a stoma reduced in size but adequate. The success of this simple manœuvre is clear proof that the kink in the jejunum at its attachment to the lesser curve was indeed the cause of the obstruction.

The advantage of this method is that the alkaline juices continue to bathe the gastrojejunal junction and protect it from ulceration. If the old anastomosis does not lend itself to this procedure it is better to separate the parts entirely and make a new one with the method described in this paper.

Some Techniques of Gastrectomy

Although there are few more grateful patients than those who have been relieved of their afferent-loop obstruction, it would clearly have been better if the original operation had not caused it. In carrying out a partial gastrectomy the surgeon cannot avoid exposing the patient to dumping symptoms. He can, and should, however, see to it that his operation does not add any element of obstruction at the stoma which may produce the much more distressing and intractable effects of bile distension in the afferent loop. It is therefore relevant to examine the Polya operation and some of its modifications with this matter in mind. The historical approach is illuminating. Polya's (1911) original paper described a limited resection of the stomach with implantation of the whole width of the gastric stump into the side of the jejunum behind the transverse colon.

Full-width Stoma

The first modification of this procedure followed the realization that anastomotic ulceration could result from insufficient resection of the stomach in duodenal ulcer cases. At least three-quarters must be removed. To do this the line of transection must cross the lesser curve about 1½ in. (3.8 cm.) below the cardia. This level is roughly 3 in. (7.5 cm.) above the origin of the jejunum, and if the intestine is hitched up to this point the obstructing kink illustrated in Fig. 1 is apt to form there. In a retrocolic anastomosis the acuteness of this angle may be increased by the snaring effect of the hole in the mesocolon. The edges of the hole should of course be sutured to the stomach well above the line of anastomosis, but it is often difficult to do this at the highest point, where the kink lies.

Valved Anastomosis

Early in the study of dumping after gastrectomy it was observed that a barium meal could pass backwards into the afferent loop, and the conclusion was drawn that this was the cause of the symptoms (Ogilvie, 1935; Mimpriss and Birt, 1948). A "valved" anastomosis was therefore designed to prevent this happening. The stoma was restricted to the lower half of the cut end of the stomach and the "valve" was formed by closing the upper half and suturing the contiguous jejunum to it as far as the lesser curve. The technique succeeds completely in its object, not indeed by any valve mechanism but by establishing the same obstructing kink at the high point at the lesser-curve attachment of the jejunum.

The conception of a valve runs counter to all accepted principles of physiology. The idea that some sort of *vis a tergo* would propel the food emerging from the stomach in one direction ignores the fact that peristalsis is the only means of moving the contents along the gut. It discounts the normal physiological process of a to-and-fro mixing of food and bile in the duodenum. Its acceptance for so long must be viewed as a measure of the concern felt by surgeons about the apparently intractable nature of post-gastrectomy syndromes.

Antecolic Anastomosis

This method of approximating the stomach and jejunum seeks to avoid the constricting effect of the hole in the mesocolon which may arise with the retrocolic anastomosis. It is easier to do, and also easier to undo if ulceration should arise at the stoma. Colonic involvement in the latter event is also less likely than after a retrocolic anastomosis.

In this operation the jejunum is brought out from its natural position under the mesocolon and carried in front of the colon and omentum to be attached to the stump of the stomach under the liver. Two serious effects may result from this dislocation of the gut. One of these is the obstruction which may follow adhesion of coils of efferent jejunum in the region of the spleen. Visick (1948) described this condition with its symptoms and radiological appearances and mentioned that he was forced to operate on five cases.

The other disadvantage lies in the new possibilities of obstruction inherent in the creation of the gastro-jejunal sling in front of the other viscera. This sling is fixed at each end, but free to swing and rotate in the middle. Behind it lies a foramen. With such an arrangement the stage is set for a loop of gut to slip behind the sling and become obstructed. A more subtle form of obstruction results from partial rotation of the sling (Fig. 2). This movement approximates the afferent and efferent jejunal loops, the angle between them at the lesser curve attachment becomes more acute, and the obstructive effect is enhanced.

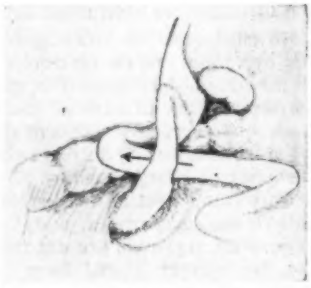

FIG. 2.—Antecolic anastomosis showing rotation with impaction of jejunum.

These events may occur at any time after the creation of the sling. If they arise in the immediate post-operative period the distension may rupture the duodenal stump (Stammers, 1952; Warren, 1954; Henson, 1955; Simon, 1956; Watson, 1958). In one series of cases the mortality due to ruptured duodenal stump was 3.8% (Goligher *et al.*, 1956). The cause of this grave complication is not sufficiently recognized. Technical instructions on partial gastrectomy stress the need for secure closure of the duodenal stump with unabsorbable sutures. This is misleading. The need is to remove the possibility of obstruction which causes the burst and which is increased unnecessarily by placing the anastomosis in front of the colon.

The obstructive events, however, may not arise until later, when the suture lines are healed. They now take the form of bile vomiting and so-called intractable dumping already described. Wells and MacPhee (1954) have described how this may occur months or even years after the operation.

There are therefore two items among techniques of partial gastrectomy which tend to produce post-operative obstruction: they are hitching of the afferent jejunum to the lesser-curve end of the gastric stump, and the placing of the anastomosis in front of the colon. The second of these may aggravate the first.

Retrocolic No-loop Gastrectomy

The upper jejunum arises from a posterior fixed point under the transverse mesocolon, to which it is attached by the ligament of Treitz. From this origin the gut falls away to the left renal pouch, where it lies in a sac bounded above by the mesocolon, with colon to the left, and colon and omentum in front. Within this enclosure the mass of guts can squirm and wriggle freely in the process of digestion.

Many gastrojejunal anastomoses interfere with this arrangement by the creation of a second fixed point in the jejunum by hitching it up to the gastric stump. We have seen that obstruction can result from this, either at the angle of attachment or behind the afferent loop so created. In the operation described below both these effects are avoided by placing the anastomosis at the natural fixed point at the attachment of the ligament of Treitz. A special preparation of the gastric stump is required to bring the gastric stoma down to the required level.

The steps of the operation are illustrated in Fig. 3. The division and closure of the duodenum and the mobilization of the body of the stomach are carried out

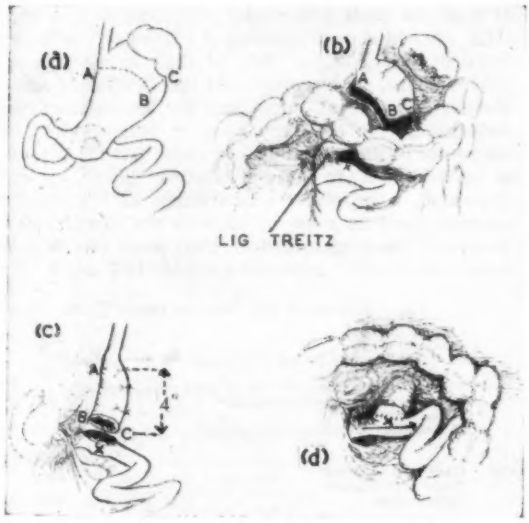

FIG. 3.—Retrocolic no-loop anastomosis.

in the usual way. The fundus of the stomach is now freed from its attachments by dividing all the vasa brevia and peritoneal membranes to within half an inch (1.3 cm.) of the oesophagus. The line of section across the stomach is made in an angular fashion as shown at ABC in Fig. 3 *a* and *b*. AB is closed by sutures: BC is to be the stoma. By these means the gastric remnant is converted into a freely mobile tube about 4 in. (10 cm.) long. This is now swung down from its original horizontal position to a vertical one, bringing the stoma BC down to the level of the origin of the jejunum (Fig. 3 *c*).

The ligament of Treitz is now identified and an opening is made in the mesocolon continuous with it. The end of the tube of stomach is brought through this hole and anastomosed to the side of the jejunum at its origin (Fig. 3 *d*). With this method of reconstruction there is no afferent jejunal loop, the stoma being in effect an extension of the ligament of Treitz. There is no drag on the mesentery of the jejunum, which falls away to the left in the normal way. The stomach remnant is supported at either end.

Results

By dispensing with the kink and the necessity for an afferent jejunal loop this operation avoids those post-gastrectomy symptoms which are due to obstruction. These are the major ones, and during the 20 years in which it has been used by me for duodenal ulcer there have been no burst duodenal stumps and no cases of bile vomiting or of intractable dumping. The results, indeed, are comparable with those of the Billroth I operation, which has been employed during the same period for gastric ulcer. The post-operative records have been gathered over the years at a weekly follow-through department. To illustrate the results 110 consecutive cases of operation for peptic ulcer have been taken from which to compile Tables II and III. The operations in this group date from March, 1948, retrospectively in order to provide a minimum period of 10 years' observation. There was no operative mortality, but 10 patients have since died of unrelated disease. Tables II and III refer to the remaining 100

TABLE II.—*Operations Performed for* 100 *Cases of Peptic Ulcer*

Retrocolic no-loop anastomosis		54 cases
Duodenal ulcer	31	
Duodenal* and gastric ulcers	5	
Gastrojejunal ulcer	12	
Gastric ulcer	6	
Billroth I anastomosis		42 ,,
Gastric ulcer	39	
Gastric* and duodenal ulcer	3	
Antecolic anastomosis		4 ,,
Duodenal ulcer	4†	

* This lesion predominating. † One patient with bile vomiting.

patients. Table II sets out the actual operations performed. The standard procedures have been the retrocolic, no-loop gastrectomy for duodenal ulcer, and the Billroth I for gastric ulcer. There have been two exceptions to this rule: where suspicion of malignancy in a gastric ulcer has required removal of the first part of the duodenum the jejunal anastomosis has been substituted for the Billroth; in duodenal cases where the mesocolon has been too short or too distorted to allow a retrocolic anastomosis, an antecolic one has been done instead. Four antecolic anastomoses have been made for this reason, and one of these patients suffered mildly from bile vomiting afterwards.

The object of Table III is to illustrate the post-operative capacity for work and for meals. No

TABLE III.—*Ten-year Results of Gastrectomy for Peptic Ulcer*

	Billroth I 42 Cases	No-loop Retrocolic 54 Cases	Total %
Recurrent ulcer	0	0	0
Off work	0	0	0
Change to light work	3	9	12·5
Diarrhoea	0	1	1
Bile vomiting	0	0	0
Meals:			
Fail to eat meat	0	0	0
No sweet course	19	25	46
,, liquids	22	32	56
Discomfort with full meal	18	31	51

patient failed to return to work after the gastrectomy, although 12 changed to a lighter job. At meal-times all the patients can take meat and vegetables. About half of them, however, restrict the size of the meal, refrain from sweet foods, and do not drink with their food. The most frequent problem in the follow-through department is how to advise a patient who has to limit the size of his meals to take sufficient food in the circumstances of his employment. Most of the patients improve on their pre-operative weight, but few regain the pre-ulcer weight of their youth. Some of them appear less robust than a normal person, but none has the distress of an intractable dumping syndrome.

Conclusion

In making this contribution I have communicated with many colleagues, who have kindly informed me of the techniques of gastrectomy which have been associated with their published papers dealing with post-gastrectomy syndromes. In all of these techniques the jejunum is fixed to the lesser curve of the gastric stump, either by a valve or by a full-width stoma. It is difficult to avoid the conclusion that this step is the cause of subsequent obstructive phenomena. This conclusion is supported by the results of the no-loop retrocolic gastrectomy described.

Summary

The inadequacy of simple gastro-enterostomy for duodenal ulcer at the present time is demonstrated.

The fallacy of judging operations for peptic ulcer on short-term results is illustrated.

The distinction between the dumping syndrome and post-operative obstructive phenomena is discussed.

Some techniques of gastrectomy are analysed with regard to post-operative obstructive effects.

Reasons are given to suggest that attaching the jejunum to the lesser curve of the gastric stump is the cause of major post-gastrectomy syndromes. A full-width stoma or valve is the technique most likely to do this. Further obstruction may result from the antecolic position of the stoma.

A method of gastrectomy is described in which a tube of fundus is mobilized to reach down to an anastomosis at the ligament of Treitz. The creation of an afferent jejunal loop is thereby avoided. No major post-gastrectomy symptoms have occurred in a 10-year follow-up of the results of this operation.

I would like to put on record my thanks for the help I have received from Mr. J. R. G. Bastable, senior registrar, and Mr. Michael P. Ward, registrar, of the London Hospital, in analysing the records of the follow-through cases to provide the material for the tables in this paper.

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ALIMENTARY BLEEDING OF OBSCURE ORIGIN

A FOLLOW-UP STUDY AND COMMENTARY

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All clinicians will have had the experience of treating patients with alimentary bleeding and in whom routine clinical and radiological tests have failed to reveal the cause. The purpose of this paper is to review the possible reasons for bleeding in such cases.

In all large series of patients with gastro-intestinal bleeding, such cases account for about 15–25% of the total series: thus Schiff (1947) recorded 26.4% among 325 admissions, and, on reviewing this and a further series of cases in 1952, still noted 20.6% of cases with no cause of their bleeding demonstrated. Palmer (1952), despite a vigorous diagnostic policy, found that 14% of his cases still evaded diagnosis several weeks after admission. Reviewing 1,252 cases, Birke and Engstedt (1956) found 15% of their cases without a proved source of bleeding. At the Central Middlesex Hospital, 20% of all admissions for haematemesis and melaena did not have any *x*-ray or other evidence for the source of their bleeding. In such cases the physician is anxious not to miss a chronic ulcer or, more important, a neoplasm which might at that time be operable, and he must be alert to the rare causes of bleeding. The diagnosis of the total series of admissions from 1941 to 1957 inclusive is shown in Table I.

TABLE I.—*Proved and Probable Peptic Ulcer*

Chronic gastric ulcer	423
Duodenal ulcer	844
Post-operative group (gastro-enterostomy or partial gastrectomy)	168
"Acute lesion" group (214 had an acute gastric erosion or ulcer seen gastroscopically)	720
Hiatus hernia	47
Unclassified (incomplete investigations)	96
	2,298
Carcinoma ventriculi	57
Portal hypertension	75
Other causes	96
	2,526

This problem can be studied in three ways. First, by reviewing the follow-up results to see if any subsequent causes of bleeding appear in those with initial *x*-ray negative findings and without any obvious clinical explanation; secondly, by reviewing our knowledge of uncommon causes so that vigilance can be increased; and, thirdly, by studying further possible precipitating causes of gastroduodenal haemorrhage.

Follow-up Studies

At the Central Middlesex Hospital nearly all the patients with gastro-intestinal bleeding are admitted under the department of gastro-enterology. Such

patients may be classified as suffering from haematemesis, melaena (altered blood in the stools), or rectal bleeding (fresh blood in the stools), or as a combination. Apart from clinical examination, the investigation of these patients included a routine barium-meal study, usually done within a week of admission, and sometimes a follow-through barium-meal examination of the small intestine and barium-enema investigation. As a routine, patients with gastro-intestinal bleeding are gastroscoped unless there is some definite contraindication. In cases of melaena or rectal bleeding sigmoidoscopy is routinely performed. Other investigations which are relevant to a particular case will be made, such as oesophagoscopy, estimation of liver function, etc.

During the period 1950–5 151 patients were admitted in whom no cause for the intestinal haemorrhage could be detected. Nine of these cases with melaena or rectal haemorrhage are included despite the *x*-ray finding of colonic diverticulitis, as there is always some doubt about the wisdom of attributing haemorrhage to diverticula alone unless red blood is passed. During the same period there were 1,051 admissions with bleeding from acute or chronic peptic ulceration. Thus for every seven cases admitted with bleeding due to ulcer there was one in which the cause up to the time of discharge remained unestablished.

Of this series of 151 the ultimate fate of nine remains unknown, but the remaining 142 cases have been followed over a period varying from three to seven years (Table II).

TABLE II.—*Method of Follow-up Examination in* 151 *Patients*

Patients known to have died of non-related causes ..	12
,, readmitted for subsequent symptoms	15
,, attending for out-patient interview and subsequently volunteering for barium-meal studies ..	90
Patients reporting by letter alone	25
,, not traced	9

Results

In Table III are listed the subsequent diagnoses which have been made and which may have accounted for the original haemorrhage.

It would appear that in about a quarter of the cases of intestinal bleeding in which no lesion is detected at the time of haemorrhage subsequent investigations will reveal what may have been the cause. Perhaps of equal interest are the remaining 77% of patients who

TABLE III.—*Lesions Subsequently Found in* 142 *Patients Followed Up*

No subsequent diagnosis achieved			109
Subsequent lesion found			33
	Type of Lesion Found	M.	F.
Peptic ulcers	Chronic gastric ulcer ..	2	2
	,, duodenal ,, ..	10	7
Malignant neoplasm	Carcinoma of stomach	3	1
	,, ,, colon ..	1	2
	,, ,, pancreas	1	0
	,, ,, small intestine	0	2
Miscellaneous	Meckel's diverticulum ..	1	0
	Hereditary haemorrhagic telangiectasia ..	0	1

never have an adequate cause for their haemorrhage demonstrated and who must remain a diagnostic mystery or be labelled with speculative diagnoses such as "gastritis" or "acute gastric erosion."

Peptic Ulcer Group

The most common cause found in patients with gastro-intestinal bleeding of obscure origin when re-examined or readmitted was peptic ulceration. This occurred in 21 patients, with 4 gastric ulcers and 17 duodenal ulcers, thus reflecting the usual excess of duodenal ulcer. It is assumed that the initial haemorrhages may have been due to acute gastric or duodenal erosions undetectable by *x*-ray examination, and it is possible that these lesions may later progress to chronic gastric and duodenal ulcers. In a follow-up of patients with acute gastric ulcers Avery Jones and King (1953) have shown by gastroscopic examination that males in particular tend to return with chronic gastric ulcers. Probably what applies to the stomach may also apply to the duodenum and to acute duodenal lesions, which presumably occur not infrequently in patients with gastro-intestinal bleeding and progress to identifiable duodenal ulcers.

Neoplasm

No fewer than 10 patients were subsequently shown to be suffering from malignant neoplasm of the stomach in 4, the colon in 3, the pancreas in 1, and the small intestine in 2. In a similar follow-up study in Sweden, Birke and Engstedt (1956) found 24 patients with malignant tumours among 191 in whom the source of bleeding had not been determined during the initial stay in hospital.

Gastric Carcinoma.—In a review of 305 patients with gastric carcinoma who underwent gastroscopy LaDue *et al.* (1950) showed that examination with the flexible gastroscope was nearly as successful as radiology in the detection of the growth, and when both methods were used 96% of lesions showed as an abnormality in one or other of these methods. Carcinoma in the fundus of the stomach may easily be overlooked on radiological examination. A soft-tissue mass is occasionally seen to deform the gastric air bubble, but barium may sink below the lesion quickly and its presence may therefore not be detected. It is in such a situation that gastroscopy can be of value, as the gastric fundus is well visualized; a fundal neoplasm must not be missed, as such growths may be as amenable to surgical removal as those nearer the pylorus.

Growths in the more distal parts of the stomach tend to be more readily detectable on barium-meal examination, and gastroscopy is less likely than radiology to detect lesions in this situation. It is therefore of some interest to re-examine the evidence in the four cases subsequently found to have gastric neoplasm. Two of the patients were not gastroscoped, and in the other two abnormalities were noted but the wrong conclusions had been drawn. In one case, that of a man of 66, the significance of the "coarse folds" seen gastroscopically was not appreciated at the time; in the second the presence of a subsequently proved duodenal ulcer and the appearance of mammillation of the gastric mucosa (a common finding with the hypersecreting stomach in duodenal ulcer) misled the clinicians into believing that intestinal bleeding was probably from a duodenal ulcer, whereas a gastric carcinoma may have been present.

Pancreatic or Ampullary Carcinoma.—The erosion of a pancreatic or ampullary neoplasm into the duodenum may cause frank alimentary bleeding. Rarely, the invasion and the occlusion of the splenic vein by such lesions may cause haemorrhage from oesophageal varices. Unfortunately, the detection of pancreatic neoplasm without jaundice may be difficult, and in the absence of radiological evidence the help afforded by tests of pancreatic function may be restricted. With an ampullary carcinoma there may

be intermittent pale stools, and bleeding may impart a peculiar silvery appearance to the stool. The alkaline phosphatase is often raised, with ampullary obstruction, and intravenous cholangiography may show dilated bile ducts.

Tumours of Small Intestine.—One patient, a woman aged 65, who bled in 1952, returned in 1957 with iron-deficiency anaemia and later with vomiting, and was found to have carcinoma of the jejunum. The second patient was a woman aged 52 who bled in 1950 and had a further melaena later the same year and again in 1951. At laparotomy a leiomyoma of the duodeno-jejunal junction was found.

Carcinoma of Colon.—Melaena may arise from a right-sided large-bowel tumour, but a carcinoma anywhere may result in activation of a peptic ulcer. The really difficult diagnostic cases are those in which a duodenal deformity is noted radiographically and the colonic lesion missed altogether unless looked for because of persisting occult blood in the stools, low-grade fever, and a raised E.S.R.

Other Less Common Causes of Bleeding

The follow-up study of these 142 cases did not uncover all the rare causes of bleeding, and the following causes are briefly noted to encourage the constant vigilance needed to establish an accurate final diagnosis. Most of these less common causes have now been detected in our main hospital series.

General medical conditions include pseudoxanthoma elasticum, food allergy, periarteritis nodosa, Henoch–Schönlein disease, malignant hypertension, chronic nephritis, myelomatosis, amyloidosis, those associated with cerebral vascular accidents, and factitious or self-inflicted lesions.

Pseudoxanthoma elasticum (Grönblad–Strandberg syndrome) is a disease characterized by widespread abiotrophy of elastic tissue throughout the body. The salient features are: (1) The appearance of angioid streaks in the retina. (2) The development of laxity of the skin, particularly in the neck, axilla, and groin. There is a yellowish discoloration of the skin in these regions, hence the term "pseudoxanthoma." Histological changes show fragmentation of elastic tissue with calcification. (3) Visceral manifestations which include recurrent alimentary bleeding from rupture of a blood vessel in the stomach or intestine. The diagnosis may be suspected from the characteristic appearance and elasticity of the skin of the neck and axilla. No cases were diagnosed in the main series, but three have been seen when investigated after a haemorrhage elsewhere.

Food allergy also has not been specifically diagnosed in this series, but one individual is known to us who has had a haematemesis every time he has eaten onions. The relationship between general medical conditions and alimentary bleeding has been well reviewed by Brick and Jeghers (1955).

The possibility of blood diseases must always be carefully considered. Haemophilia, thrombocytopenia, thrombasthenia, and myelosclerosis may not present any real diagnostic problems, but von Willebrand's disease may do so. This is a familial bleeding tendency inherited as a dominant. Nose-bleeding and easy bruising are common manifestations, but gastro-intestinal haemorrhage occurs in about 15% of patients. Excessive bleeding may occur from cuts, but operations are usually not complicated by serious bleeding. The diagnosis should be considered particularly in patients with recurrent episodes of bleeding in whom there is a history of easy bruising and in whom there is a family history of bleeding. These patients have a normal platelet count and morphology, and normal clotting, clot retraction, and prothrombin time. The abnormal findings are a positive Hess test in about half the cases. Bleeding-time is variable at different times and at different sites, but is greater than 15 minutes at some time in most patients. The antihaemophilic globulin in many patients is low and within mild haemophilic range, and the prothrombin consumption is poor in half of them. Sometimes the capillary morphology with contraction is abnormal. It is a disorder which has some features suggesting a disturbed clotting mechanism (low antihaemophilic globulin and abnormal prothrombin consumption) and some features suggesting a capillary with platelet defect (prolonged bleeding-time and positive Hess test).

Rare Local Alimentary Causes

Simple tumours of the alimentary tract are a small but important group. Leiomyomata may occur in the small intestine as well as in the stomach, where they are usually easily diagnosed. In the small intestine, however, they may easily escape detection. In one patient it was found only at the third laparotomy performed at the time of bleeding and when bleeding into the tumour made it palpable for the first time at the duodeno-jejunal junction. Neurofibromata are even more rare, but skin lesions may indicate their possible presence.

There are two important groups of diverticula of the alimentary canal—Meckel's diverticula and colonic diverticula. The presence of red blood with a melaena stool is an important pointer towards the possibility of bleeding from a Meckel's diverticulum, and localized tenderness in the lower abdomen, particularly on the right side, is confirmatory evidence. The presence of a Meckel's diverticulum does not mean that it has been the cause of bleeding, and some evidence of associated peptic ulceration is needed. In one patient in whom a Meckel's diverticulum was discovered the cause of bleeding was finally diagnosed as a rare bleeding diathesis.

Brisk severe bleeding with passage of red blood will occur from a bleeding colonic diverticulum. The haemorrhage in such cases probably occurs from a small abscess in relation to the diverticulum. The bleeding may be severe enough to need urgent laparotomy. Diverticula in the oesophagus, stomach, duodenum, and small intestine are usually incidental findings, and some other cause for the bleeding should be sought for, but occasionally it may be possible to prove that a duodenal diverticulum or an intestinal diverticulum with enteroliths has caused the haemorrhage. Herrington (1958) reports a case of massive haemorrhage from benign ulceration in a primary duodenal diverticulum.

Local vascular causes affecting arteries, veins, or capillaries are occasional causes of serious gastro-intestinal bleeding. Arteriosclerosis of gastric arteries is uncommon (Osborn, 1954) and is not normally found in the exposed vessels in the floor of ulcers. Nevertheless, gross localized tortuosity of gastric arteries may occur with extrusion of a vessel through the mucosa. One such case in this series was diagnosed

gastroscopically. This type of circoid aneurysm has been reported by Donaldson and Hamlin (1950). True aneurysms, arteriosclerotic, mycotic, or syphilitic, are all occasional causes when eroding the alimentary tract. An aneurysm bleeding into the biliary tract may also cause haematemesis and melaena. Aneurysm of the hepatic artery rupturing into the bile duct has been reported by Malloy and Jason (1942), Gordon-Taylor (1943), and McGregor (1952). In these patients pain simulating gall-stones, haematemesis, and jaundice may occur as a triad. Severe bleeding can also be associated with a fistula between a gall-bladder containing calculi and the duodenum (Moore, 1952). This can be associated with acute duodenal obstruction. Other rare causes of bleeding into the alimentary tract from biliary and pancreatic sources have been recorded by Kerr, Mensh, and Gould (1950).

Hereditary haemorrhagic telangiectasia, a capillary abnormality, is an occasional cause of bleeding from the stomach and intestine, usually of only mild or moderate severity, but it can be fatal. It was diagnosed twice in this series. The history of epistaxis is an important clue to its diagnosis, but a family history is not always present.

Haemangiomatosis, localized or diffuse, may cause recurrent bleeding, and five anatomical varieties are described by Kaijser (1936). Sometimes the lesions are too extensive to remove, but multiple haemangiomas in the small intestine have been removed (Heycock and Dickinson, 1951) and also from the large bowel (Babcock and Jonas, 1950). Rider, Klotz, and Kirsner (1953) have reported gastro-intestinal bleeding in a patient with venocapillary ectasia in the pyloric antrum, with large, thin-walled blood vessels in the mucosa associated with severe localized gastritis. Trauma to the oesophagus from the strain of vomiting must be kept in mind (Mallory-Weiss syndrome). These patients give a story of vomiting food first, followed by fresh blood.

Salicylates and Alimentary Bleeding

The third aspect of the problem of "*x*-ray negative" haemorrhages relates to the role of salicylates in precipitating alimentary bleeding. In a proportion of patients in whom a barium-meal examination reveals no abnormality, it has been known for some years that there is the possibility that acetylsalicylates may be responsible for inducing an acute erosive lesion of the stomach. Working in this department, Alvarez and Summerskill (1958) have made a very careful study of this subject by extracting an accurate history of salicylate consumption before 103 admissions for gastro-duodenal bleeding and comparing it with an out-patient control group. Their control group consisted of patients attending the hospital for investigation of dyspepsia, and the pattern of ulcer dyspepsia corresponded very closely with the final diagnosis of patients admitted for haematemesis. If the ulcer-prone cases are more likely to be upset by salicylates than the non-ulcer group, this is clearly a much better control group than other emergency admissions. They found that 49 out of 103 admissions for haematemesis and melaena had taken a salicylate preparation during the 24 hours preceding admission, compared with only 7 of the out-patient control group. Detailed inquiry about the reason for taking aspirin did not suggest that the symptoms of bleeding accounted for this excess. Further confirmation of the possible adverse local gastric effect of salicylates came from their observations of the effect of salicylates on the stools when tested for occult blood, and it was noted that aspirin produced a much higher proportion of positive stools than other non-salicylate analgesics.

It was concluded that aspirin plays a definite part in precipitating gastro-duodenal bleeding, confirming the previous studies of Muir and Cossar (1955), and that this mechanism makes a significant contribution to the number of "*x*-ray negative" admissions for haematemesis and melaena, perhaps even as much as 40% of this group.

Investigation of Gastro-intestinal Bleeding of Obscure Origin

The clinician is not infrequently placed in a situation where the routine clinical procedures and investigations have failed to reveal the cause of bleeding.

The personal history should be reviewed to find out if there had been any major emotional crisis in the few days preceding the bleeding—a common finding with acute ulcers. The next step is to check carefully the patient's history and family history for a tendency to bleed, and the possibility of recent medication with aspirin, cortisone, or phenylbutazone must be ascertained. The mode of onset of bleeding should be recapitulated, with special thought to the possibility of Mallory–Weiss syndrome or Meckel's diverticulum. The physical examination of the patient should be repeated, looking with great care for any cutaneous evidence of cirrhosis hepatis. Splenomegaly is a constant accompaniment of portal hypertension and is masked only by obesity or ascites, and in itself raises the possibility of cirrhosis hepatis. The skin should be inspected for evidence of congenital defects such as pseudoxanthoma elasticum, neurofibromatosis, or haemangiomata. The elasticity of the skin of the axilla and neck should be specially noted.

The possibility of hiatus hernia may need further checking if the radiological report is incomplete in this respect. The need for gastroscopy should be borne in mind.

The extent of further investigation will rest mainly on the clinical review of the case, and one will be biased in favour if the history has any unusual features, such as atypical pain and loss of weight. The most important indication for further *x*-ray examination and endoscopy is the finding of persistently positive occult blood in the stools. This will need further barium-meal, small-intestine meal, and barium-enema studies and liver-function tests. A raised alkaline phosphatase and dilated bile ducts may be found associated with an ampullary carcinoma. If there is still no indication of the cause of bleeding, some information about the level of origin may be obtained by swallowing radio-opaque string (Rappaport, 1955) overnight or by sampling the small intestine at various levels with a Miller–Abbott tube. With unexplained and persistently positive stools it is really necessary to proceed to a laparotomy. When there have been repeated episodes of bleeding it is preferable to wait for a further episode and then to undertake laparotomy at the time of bleeding. It is most important that the stomach should be opened and carefully inspected at the time of operation. It is often quite impossible to feel acute ulcers from the peritoneal surface. Sometimes the exposed vessel may be felt like a lead shot on palpation of the mucosa through a gastrostomy.

Summary

A follow-up is presented of cases of *x*-ray negative haematemesis and/or melaena. Among 142 patients followed up for three to eight years there were 33 (23%) in whom a positive diagnosis was subsequently made and which may have explained the original episode.

The diagnoses subsequently made were chronic gastric ulcer in 4, duodenal ulcer in 17, carcinoma of stomach in 4, carcinoma of colon in 3, carcinoma of pancreas in 1, carcinoma of small intestine in 2, Meckel's diverticulum in 1, hereditary haemorrhagic telangiectasia in 1.

Among the less common causes special attention is drawn to pseudoxanthoma elasticum, von Willebrand's disease, diverticulosis of the colon, and the Mallory–Weiss syndrome.

Aspirin is thought to play a very significant aetiological part.

The method of investigation of these cases is discussed in detail.

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"It followed naturally that the [New Mental Health] Bill took shape from [the Royal Commission's] recommendations; and now the title has arisen from the common euphemism of saying 'health' when we mean 'illness'; one M.P. in fact said, 'There are few subjects which cause so much distress to so many people as mental health.' (Euphemisms were of course well known to the Greeks, who called the Furies the Eumenides or kindly ones.) To object to this may seem trivial and hair-splitting. But it is in fact highly important, for there is a danger that many members of the public, and perhaps even Members of Parliament, will be misled by the title into a state of complacent satisfaction that they have now produced a finer mental health service than any other country—and therefore need do no more. They are in process, no doubt, of improving the service for mental illness: but no service for mental *health* exists yet, and the Bill makes no real proposals towards it. (The Greeks did not deceive themselves that the Furies really were kindly.)" (Editorial, *Mental Health*, **18**, 1.)

POST-VAGOTOMY DIARRHOEA: ITS CAUSE AND PREVENTION

BY

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Long-term studies of the results of vagotomy with gastric drainage (Burge and Pick, 1958) have shown that the operation is better than gastrectomy in the surgical treatment of chronic duodenal ulcer. In their work these authors found that a change in bowel habit after vagotomy was the only feature which could possibly detract from the operation. Of their patients 30% showed some small change on direct questioning. Many patients were previously constipated and welcomed the slight looseness which followed operation. Others, however, found themselves confronted with a real disability marked by early morning diarrhoea with urgency. A few have shown severe disabling diarrhoea. Our own long-term studies prove that in most cases the symptom is permanent. At one time we felt that, because of post-operative diarrhoea, the operation of vagotomy might not come to take its place as the standard surgical procedure.

Up to now the cause of this diarrhoea has been unknown. Most authors have believed that these symptoms are due to infection consequent upon gastric hypoacidity or to gastric stasis.

During our studies we found that extirpation of the coeliac plexus in the dog caused diarrhoea (Von Mering and Aldehoff, 1899). It seemed to us that vagal denervation of the coeliac plexus might be the cause of post-vagotomy diarrhoea in man.

No worker has published, as we do now, two series of cases, one with the coeliac division of the posterior vagus intact and the other with the vagal supply of the coeliac plexus interrupted by division of the posterior vagus above the origin of its coeliac branch.

We have found by stimulation tests (Burge and Vane, 1958) in animals and on man that preservation of the coeliac division of the posterior vagus does not interfere with complete gastric vagotomy.

Although a few important papers have described the anatomy of the abdominal vagus (McCrea, 1924, 1926), our own dissections in the post-mortem room have brought to light anomalies, not mentioned in these papers, which are important now that vagotomy has become the standard surgical procedure.

We have found that the coeliac division of the posterior vagus usually arises at a level below the gastric cardia (Fig. 1). In this case when the posterior vagus nerve is divided denervation of the coeliac plexus must occur. Sometimes the coeliac branch was found to arise at a higher level, though still below the diaphragm (Fig. 2). In such a case it would seem possible that when a posterior nerve trunk is overlooked the coeliac innervation may be preserved. In some cases we found that the coeliac division arose within the chest and passed, closely applied to the abdominal wall, the coeliac plexus (Fig. 3). It seems likely that this nerve must sometimes

be missed during standard vagotomy. Although the coeliac division may arise in this way above the diaphragm it may give gastric branches which need division.

Operative Procedure

Using a foot-down tilt, the abdomen is opened by a high left paramedian incision and the left lobe of the liver mobilized in the usual way and retracted to the right. A small incision is made in the peritoneum to the left of the oesophagus and the right index finger passed behind the oesophagus to make a hole through the peritoneum on its right. In doing this the coeliac division of the posterior vagus must be felt like a string as it passes the posterior abdominal wall. The anterior vagus nerve or nerves are dealt with by complete section. It is useful to pass a thread round the main posterior vagal trunk for traction. A hole is made in the small omentum, and it is divided upwards from the pyloric region to the diaphragmatic hiatus.

The left gastric artery and vein are divided separately between ligatures. This step in the operation is made easier if the assistant stretches the stomach by holding the fundus outside the wound. We at one time considered an attempt to divide the gastric branches of the posterior vagus while retaining the left gastric vessels as well as the coeliac branch of the nerve. However, the presence of many small branches arising from the coeliac division and passing to the stomach with the left gastric vessels made us decide to divide the left gastric artery and vein. We have always proved that gastric nerve section is complete by test before performing posterior vertical gastro-enterostomy.

Clinical Findings

From long-term studies carried out by Burge and Pick it was found that 30% of their series of 301 patients who had had vagotomy and gastro-enterostomy replied "Yes" to the question, "Do you have diarrhoea or loose motions?" This series was drawn from many cities in England, and it is interesting to note that the incidence was the same in each city.

Before performing this selective vagotomy we had available for comparison 25 consecutive cases of vagotomy the completeness of which was proved by test and in which no attempt had been made to preserve the coeliac division. Since using this selective operation we have carried out another series of 25 consecutive cases in which the coeliac division was preserved while maintaining complete gastric section. The incidence of diarrhoea in these two series was determined, and is set out in the table. An occurrence of 10 cases (40%) in the first series is compared with no occurrence whatsoever in the second series.

Incidence of Diarrhoea

	No. of Cases	With Diarrhoea	With Severe Diarrhoea
Series 1 (coeliac nerve cut) ..	25	10 (40%)	2 (8%)
,, 2 (,, ,, intact) ..	25	0	0

Discussion

As the operation of vagotomy with gastric drainage has become more popular in recent times, surgeons using it have become more aware of post-operative diarrhoea, which although usually mild can sometimes be severe. We thought that this symptom might be caused by vagal denervation of the coeliac plexus, and decided that the simple method of comparing the two series of cases, one with the coeliac division divided and one with it intact, was the only satisfactory method of proving or disproving our theory.

In each centre in England where the operation was done, even when the series has been small, there has been a very constant incidence of diarrhoea on direct questioning. We must stress that it is unusual for the patient to complain of diarrhoea without this direct question. In view of this constant figure of 30% in the total series of Burge and Pick and in the figures from each centre, and the comparable figure of 40% in our own series, we conclude that the complete absence of diarrhoea in the 25 cases in which we have preserved the coeliac division must be significant.

Summary

The incidence and severity of post-vagotomy diarrhoea are discussed. Strong evidence is put forward for the first time that this condition is caused by denervation of the coeliac plexus when the posterior vagus nerve is divided. Important anatomical anomalies of the origin of the coeliac divisions are described. The technique of vagotomy with preservation of the coeliac

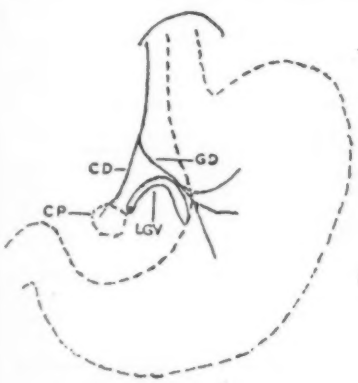

FIG. 1

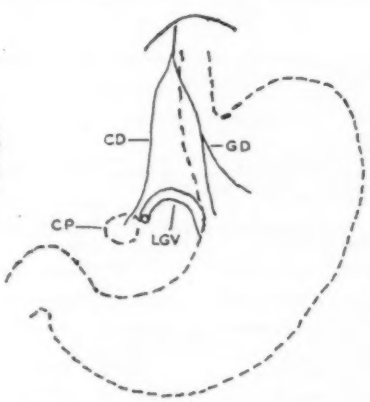

FIG. 2

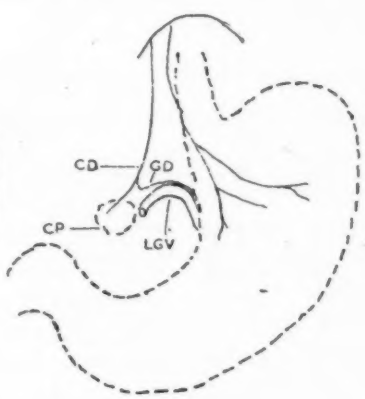

FIG. 3

CD=Coeliac division. CP=Coeliac plexus. GD=Gastric division. LGV=Left gastric vessels.

division is detailed. Complete gastric nerve section is demonstrated by stimulation.

Two series of cases are compared. Since the coeliac innervation has been preserved there has been no case of diarrhoea.

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VANCOMYCIN: REPORT ON TREATMENT OF PATIENTS WITH SEVERE STAPHYLOCOCCAL INFECTIONS

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This paper describes the use of vancomycin in the treatment of nine patients in Hammersmith Hospital who suffered from severe staphylococcal infection of the blood stream, lungs, or operation wounds.

The prevalence in hospital of strains of *Staphylococcus pyogenes* resistant to several antibiotics has led to "the present-day pharmaceutical equivalent of the Gold Rush . . . for new antibiotics" (*Lancet*, 1957). Hospital in-patients are now not uncommonly infected by strains of staphylococci resistant to four or five of the antibiotics to which this species is normally sensitive. Furthermore, all the antibiotics which can be used in the treatment of staphylococcal infections of the lungs, blood stream, or other deep-seated lesions, and which have been introduced since penicillin and streptomycin, are predominantly bacteriostatic.

The isolation of vancomycin from *Streptomyces orientalis* by McCormick *et al.* (1956) was important, for the drug is bactericidal for Gram-positive cocci (Ziegler *et al.*, 1956; Geraci *et al.*, 1956). Moreover, the numerous strains of *Staph. pyogenes* tested against it have been almost invariably sensitive (Fairbrother and Williams, 1956). As shown by Garrod and Waterworth (1956), neither cross-resistance with other antibiotics nor the development of material degrees of resistance *in vitro* has been found.

The drug is poorly absorbed from the intestine. The current preparation is too irritant for intramuscular injection, and, in any case, the drug is not well absorbed by this route. It must therefore be given intravenously.

Geraci *et al.* (1956) found that vancomycin was almost entirely excreted in the urine with a small amount in the bile and faeces. It begins to accumulate in the blood after the first two or three days' treatment.

Although direct intravenous injections can be given, there is a material risk of thrombophlebitis unless veins are used in rotation. The method of intravenous administration least likely to cause thrombophlebitis is by infusion in about 250 ml. of diluent over about 30 minutes or, where applicable, by admixture with a saline or 5% dextrose "drip." Because of the need to give the drug intravenously, and because of its toxicity (see below), vancomycin is at present mainly used for severe staphylococcal infections in hospital, and it is such a group of nine patients that is described here.

Treatment of Patients

The nine patients were not selected; they comprise all those treated with vancomycin at Hammersmith Hospital up to August, 1958, except for three patients who received the drug only when *in extremis*. Information given in the following case reports is summarized in Tables I, II, and III. Eight of the nine patients (Cases 1–8) had failed to respond to other antibiotics before vancomycin was used.

Table I shows the patients' presenting illness, the nature of the staphylococcal infection, and the response to vancomycin. Those who received an adequate course of the drug responded well clinically.

Table II indicates the antibiotic sensitivity pattern and phage type of the strains of *Staph. pyogenes* isolated and the preceding courses of antibiotics given to the patients.

Severe loss of auditory acuity followed treatment in several patients, and Table III shows the incidence and its relation to high blood urea levels.

TABLE I.—*Infections and Response to Treatment*

Case No.	Age and Sex	Admitted to Hospital for Treatment of	Site(s) of Staphylococcal Infection(s)	Response to Vancomycin Treatment	
				Clinical Response	Elimination of Infecting Staphylococcus
1	78 M	Gangrene of foot (arteriosclerotic) with mild diabetes	Transfusion and amputation wounds (leg), lungs	Rapid complete recovery	No
2	37 F	Asthma with chronic suppurative bronchitis	Lungs	Slow but good recovery from acute-on-chronic infection	"
3	19 wks. M	Paroxysmal cough	Lungs (throat swabs)	Slow but good recovery	"
4	28 F	Bilateral lobar pneumonia with anuria	Blood	" " " "	Yes
5	42 M	Bronchopneumonia with renal failure	Lungs, blood	Rapid recovery	"
6	49 M	Post-operative anuria (following partial nephrectomy)	Wound, blood	Recovery from staphylococcal infection but died of *Ps. pyocyanea* septicaemia	"
7	55 F	Oliguria and biliary peritonitis (following cholecystectomy)	Cholecystectomy wound, lungs, peritoneal cavity		No
8	73 M	Bilateral basal pneumonia	Lungs	Rapid initial improvement on vancomycin but relapsed and died when other chemotherapy substituted	No follow-up specimens seen, but presumed not eliminated
9	63 F	Persistent vomiting (due to carcinoma of stomach)	Blood		No

Table IV gives the results of serum vancomycin assays by a rapid method in a tenth patient who was anuric. The dosage of vancomycin was controlled by the assay results.

Method of Administration.—Vancomycin was given intravenously by direct injection in 20 ml. of saline over a five-minute period; by infusion in 250 ml. over a 30-minute period; or, diluted with larger volumes of saline or 5% glucose, through a vena cava catheter over several hours. The total daily dose (Table III) was 1–2 g., except for Case 3, and was given as two equal 12-hourly doses. No patient received vancomycin for longer than 15 days, and the maximum course was 22 g.

Bacteriological Methods

Bacterial strains referred to in the case notes were isolated from the patient's specimens by routine laboratory methods. The amount of growth is shown as +, ++, or +++. The sensitivity of strains of *Staph. pyogenes* to penicillin, streptomycin, tetracycline, chloramphenicol, erythromycin, novobiocin, and vancomycin was tested on nutrient agar or horse blood agar by a ditch-plate technique, using the Oxford strain of staphylococcus as a control and incubating at 37° C. for 18 hours. Sensitivity (S) or resistance (R) to each antibiotic is indicated in the case notes in the order of drug just given—for example, RRRSSS denotes that the strain was resistant to penicillin, streptomycin, and tetracycline, but sensitive to chloramphenicol, erythromycin, and novobiocin. All strains were sensitive to vancomycin; those not eliminated from the body by treatment remained sensitive. Bacteriophage typing of the strains was carried out in this laboratory by the method of Williams and Rippon (1952), using 21 phages. The types are indicated in Table II and follow the sensitivity pattern in the case notes. Serum vancomycin assays were not undertaken routinely during the treatment of these nine patients but have been introduced subsequently (see below and Table IV).

Case 1

A man of 78 with mild diabetes—admitted with arteriosclerotic gangrene of one foot. Treated for the sepsis of one toe with penicillin and streptomycin.

Day 30: Toe excised—pus yielded *Staph. pyogenes* (+++, SSSSSS, 52/52A). *Days 32–39:* Erythromycin *alone*. Progressive local and general deterioration. *Day 49:* Above-knee amputation. *Day 53:* Chest pain—myocardial infarction. *Day 57: Staph. pyogenes* (RRRSRS, 80) isolated from sputum (+) and transfusion wound (+++). The latter also yielded *Clostridium welchii*, treated with penicillin. *Day 59:* Chloramphenicol started. *Day 62:* Left basal pneumonia. Sputum yielded *Staph. pyogenes* (+++, RRRSRS, 80).

Days 62–68: Vancomycin (total 10 g.) with rapid improvement in general and local condition after first two days. *Day 64:* Type 80 staphylococcus (+++) isolated from amputation and transfusion wounds. *Days 78–80:* Improvement maintained, but type 80 organisms were still recovered from his amputation wound (+++) and sputum (++) on these two days in spite of a further course of 4 g. of vancomycin. For this reason he was transferred to a fever hospital, where he recovered after further vancomycin.

TABLE II.—*Antibiotic Sensitivity and Bacteriophage Types of Infecting Strains of Staph. Pyogenes*

Case No.	Courses of Chemotherapy before Vancomycin	*Staph. pyogenes* Strains: Antibiotic Sensitivity Pattern P	S	T	C	E	N	Phage Type
1	(1) P+S	S	S	S	S	S	S	52/52A
	(2) E, (3) C	R	R	R	S	R	S	80
2	P, T, C, Sulphonamides ..	R	R	R	S	S	S	79/47/53/77+
	E+C	R	R	R	S	R	S	*
		R	R	R	R	R	S	*
3	(1) T+sulphonamides ..	R	S	R	S	S	S	80+
	(2) E+C, (3) E+S+N ..	R	S	R	S	R	S	80
4	(1) P, (2) E, (3) S	R	S	S	S	R	S	N.T.
	(4) E+T, (5) C+T ..	R	S	S	S	R	S	N.T.
5	(1) S+C	R	R	R	S	S	S	80/53+
	(2) S+T+C, (3) E+C ..	R	R	R	S	S	S	80/53+
6	(1) E+C, (2) T+C ..	R	R	R	S	R	S	53/54/77
7	E+C	R	R	R	S	S	S	77+
		R	R	R	R	R	S	77+
8	(1) P+S	R	R	R	S	S	S	77
	(2) T, (3) C	R	R	R	S	S	S	47/53/77
9	Nil	R	R	R	S	S	S	47/53/77

P=Penicillin. S=Streptomycin. T=Tetracycline. C=Chloramphenicol. E=Erythromycin. N=Novobiocin. All strains were sensitive to vancomycin. * Strain failed to type at 1,000 × routine test dose of bacteriophages. N.T.=Not tested. In columns 3-8, under "Antibiotic Sensitivity Pattern," "S"=Sensitive.

TABLE III.—*Incidence of Deafness in Relation to Renal Function*

Case No.	Approximate Blood Urea (mg./100 ml.) during Vancomycin Treatment	Vancomycin Dosage (g.): Daily Total*	No. of Days	Total	Effect on Hearing
1	60 falling to 24 ..	1st course 1–2	6	14	Nil
		2nd ,, 2	2		
2	Normal	1st ,, 1–2	4	22	,,
		2nd ,, 2	5		
		1	6		
3	Presumed normal ..	400 mg.	5	2	,,
4	400 falling to 100 ..	1st course 2	2	13	Severe
		1	5		
		2nd ,, 1	4		
5	440 ,, ,, 310 ..	2	2	7	,,
		1	3		
6	385, reduced to 200 by dialysis, and then rising again	2	2	6	,,
		1	2		
7	380 falling to 280 ..	2	5	12	Not known
		1	2		
8	380 ,, ,, 68 ..	2	1	7	Probably deaf†
		1	5		
9	16 rising to 66 ..	2	6	12	Severe

* Given as two equal doses at 12-hourly intervals except Case 3 (=100 mg. six-hourly).
† Patient very disorientated.

TABLE IV.—*Serum Vancomycin Levels During Treatment of a Uraemic Patient*

Day:	1	2	3	4	5	6	7	8	9	10	11
Renal function: Blood urea (mg./100 ml.) ..	270	281	300	296	260	192	193	150	88	104	102
Vancomycin: Dosage* (mg.) ..	500	0	250	375	250 t.d.s.	250 b.d.	250	250 b.d.	500, 250	500, 250	250 b.d.
Route	I.V.	Vena caval drip								I.V. infusion	
Vol. diluent/dose	20 ml.	1,000 ml. (8 hrs.)							500 ml. (8 hrs.)	200 ml. (30 mins.)	
Serum vancomycin levels (μg./ml.): Highest ..	33†	12	6	10	9	16·6	20	8	14	14·4	6
Lowest ..	—	9·3	5	3·3	8	8	10·8	6·2	4·4	7	3·8
No. of assays	1	2	4	4	3	3	3	2	4	4	3

* Total amount given, 5·125 g.
† High level probably due, in part, to chloramphenicol treatment, which ceased on this day.

Whilst at Hammersmith Hospital the blood urea did not exceed 60 mg./100 ml., subsequently falling to 24 mg./100 ml. The patient was slightly hard of hearing throughout. He suffered no further loss of auditory acuity as the result of vancomycin treatment.

Case 2

A woman of 37, asthmatic since childhood, with suppurative bronchitis for 10 to 15 years, leading to pulmonary fibrosis and cavitation. Admitted for control of the infection after out-patient chemotherapy had failed (penicillin, tetracycline, chloramphenicol, sulphonamides).

Days 2–19: Erythromycin + chloramphenicol. *Day 4:* Sputum: *Staph. pyogenes* (+++, RRRSSS, 79/47/53/77+). *Days 8, 9:* Sputum: still positive. *Days 4–19:* After brief improvement her condition deteriorated, with progressive breathlessness and sputum increasingly purulent. *Days 17–19: Staph. pyogenes* (+++, now additionally resistant to erythromycin, RRRSRS).

Days 19–23: Vancomycin given by direct injection (total 6 g. only), with chloramphenicol, produced dramatic improvement, with marked diminution of sputum. *Day 23:* So much improvement that patient was allowed home for Christmas.

Readmission.—Four days later was readmitted with a relapse. *Days 1–9:* Sputum yielded a varying flora, including *Streptococcus pneumoniae* and *Haemophilus influenzae*. Steady improvement with streptomycin and tetracycline, in spite of the reappearance, on *Days 10–12*, of the original strain of *Staph. pyogenes* (+), apparently now with a less virulent role.

Days 14–24: Second course of vancomycin was given (total 16 g.) to eliminate the staphylococcus, but it was consistently isolated from six sputum specimens between *Days 15* and *28*. Her convalescence was not further hastened by the drug; she was discharged on *Day 28*. Over the next three months she remained well: the original strain of *Staph. pyogenes* was isolated occasionally from several specimens of sputum.

The patient showed no signs of renal incompetence and maintained excellent hearing both in hospital and after her discharge. There was severe thrombophlebitis of arm veins after vancomycin injections, and immediately after injections she experienced marked but very temporary hot flushes.

Case 3

A boy of 19 weeks with persistent nasal discharge and severe paroxysmal cough was admitted with pneumonia, with consolidation and, later, cavitation in the upper lobe of his right lung. Over three successive periods of about 18 days clinical improvement gave way each time to serious relapse.

Days 1–18: Remittent fever. Treated with tetracycline and sulphonamides for 12 days with some improvement. *Day 13:* Temperature rose to 103° F. (39.4° C.) and *Staph. pyogenes* (RSRSSS, 80) was isolated from a neck boil and consistently (*Days 16, 17, 18*) from both nose and throat swabs (+++).

Days 19–36: From *Days 18–30* chloramphenicol and erythromycin given and the temperature became and remained normal for about two weeks except on one occasion (105° F.—40.6° C.). Blood cultures (*Days 26, 29*) were sterile. From *Day 29* novobiocin replaced chloramphenicol. *Day 33:* Throat swab again positive (+) with the type 80 staphylococcus. *Day 36:* Patient again very ill—temperature rose to 102° F. (38.9° C.). *Pseudomonas pyocyanea* was isolated from an indwelling feeding-tube.

Days 37–57: Patient on streptomycin, erythromycin, novobiocin, and prednisolone. Temperature fell and remained down for three weeks. Throat swab cultures on *Days 42* and *54* did not yield staphylococci, but the child's condition began to deteriorate and he got much worse towards the end of this period.

Vancomycin given *Days 57–62*, total 2 g., and the child had a blood transfusion. From *Day 59* until *Day 99* there was slow but increasing improvement. The chest cleared clinically, although leaving an area of consolidation with some cavitation in the upper lobe of the right lung. On *Day 99* the boy was discharged home very well.

The child had always been somewhat mentally retarded, but it was not felt that he suffered any loss of auditory acuity. His renal function was apparently normal throughout.

Case 4

A woman of 28 with two weeks' history of fever, weakness, and vomiting after a cold was admitted to another hospital with a temperature of 102° F. (38.9° C.). Penicillin was given, but bilateral patchy pulmonary consolidation developed. Sputum culture yielded *Staph. pyogenes*. Erythromycin treatment was begun; a blood culture taken only three days later yielded an erythromycin-resistant strain of *Staph. pyogenes* (RSSSRS). Change to streptomycin and prednisolone did not halt a marked deterioration, with oliguria; the blood urea was now 205 mg./100 ml. She became desperately ill and was transferred to Hammersmith Hospital.

On admission she had consolidation of both lower lobes and rapidly became anuric. After intravenous tetracycline, erythromycin, and prednisolone (given by transfusion through a vena cava catheter) there was a dramatic improvement in her general condition and renal function. It was then learnt that the original blood culture staphylococcus had been erythromycin-resistant, so chloramphenicol was substituted. The temperature rose, and both blood culture and sputum taken on *Day 7* yielded *Staph. pyogenes* (RSSSRS).

Vancomycin given from *Days 7–14* and *18–21* (total 13 g.), and, *Day 8* only, staphylococcal antitoxin. A small quantity of streptomycin was given—because of the anuria, only intermittently. Over this period there was a gradual and sustained improvement and the blood urea fell from 400 to 100 mg./100 ml. *Day 21:* Vancomycin was replaced by tetracycline. No further infection by staphylococci occurred, but malignant hypertension had developed and she died four months later of renal failure.

The patient had become totally deaf; at first this was attributed to streptomycin, but only 2 g. had been given. The course of 13 g. of vancomycin is the more probable cause.

Case 5

A man of 42, previously fit, admitted to another hospital with pain in the right hypochondrium. His temperature was 101° F. (38.3° C.) and the blood urea 340 mg./100 ml.

He was transferred to Hammersmith Hospital; his blood urea was then 640 mg./100 ml. He was dialysed on the artificial kidney twice—on admission and on *Day 4*. His electrolytes were thereby controlled and the blood urea fell to 192 mg./100 ml. Bronchopneumonia developed and, *Days 12–17*, he was treated with chloramphenicol and a single 0.5-g. dose of streptomycin. *Day 17:* The temperature had fallen to normal, but subsequently it rose again and on *Day 23* sputum culture yielded *Staph. pyogenes* (+++, RRRSSS, 80/53) together with a lesser growth of *Ps. pyocyanea*. From *Days 24–26* the treatment given included streptomycin, intermittently and in low doses, with tetracycline and chloramphenicol, but, *Day 26*, temperature reached 103° F. (39.4° C.) and the same staphylococcus was isolated from sputum (+++) and blood culture. Meanwhile the blood urea had risen to 400 mg./100 ml. *Days 26–30:* Erythromycin and chloramphenicol given without improvement. *Day 28:* Gastrostomy performed because of vomiting. *Day 29:* Blood urea 436 mg./100 ml.

Days 30–35: Vancomycin given (total 7 g. only); temperature fell to normal and blood culture (*Day 31*) was sterile. *Day 35:* Patient disorientated and found to have severe nerve deafness, so vancomycin stopped. A single

serum vancomycin level was 20 μg./ml.—10 days later it was still 5 μg./ml. *Day 37:* Blood urea now down to 308 mg./100 ml. Urinary output improved to 3 litres daily, and on *Day 45* the blood urea had fallen to 184 mg./100 ml. Subsequently the patient again ran a fever for a few days and developed a pericardial effusion; *Staph. pyogenes* (SSSSSS, 52) was isolated (*Day 54*), and the infection was treated by tapping. No further staphylococcal infection occurred. The blood urea rose steadily from *Day 45* and reached 580 mg./100 ml. on *Day 90*, when he died of renal failure.

Case 6

A man of 49 in good health until he required a partial nephrectomy for a calculus at another hospital. He became anuric, and three days later was transferred to Hammersmith Hospital.

After admission urinary output improved on vena cava drip infusions, but by *Day 4* the blood urea had risen from 278 to 378 mg./100 ml., falling again to 274 mg. by *Day 8*. *Days 2–9:* Erythromycin and chloramphenicol given to combat some pyrexia, but from *Days 7–10* the temperature rose and reached 103° F. (39.4° C.). *Day 10:* Operation wound and urine yielded *Staph. pyogenes* (+++, RRRSRS, 53/54/77) and blood culture was also positive. Blood urea 385 mg./100 ml. *Days 10–12:* Tetracycline and chloramphenicol.

Days 10–14: Vancomycin (total only 6 g.), with chloramphenicol and hydrocortisone. *Day 12:* Temperature began to fall. *Day 13:* Blood urea 500 mg./100 ml., but this was reduced to 200 mg./100 ml. by dialysis the same day on the artificial kidney. By *Day 17*, however, it had again risen to 444 mg./100 ml., and remained at about this level till death. *Day 14:* Sputum and faeces cultures yielded *Ps. pyocyanea* (+++), but no *Staph. pyogenes* was isolated. *Day 15:* Gastrostomy operation as patient was not taking fluids by mouth. *Days 14–20:* Chloramphenicol. By *Day 17* the temperature had fallen to and remained normal, but on *Day 25* there was marked pyrexia; blood culture yielded *Ps. pyocyanea*. The infection did not respond to polymyxin and neomycin, and the patient died on *Day 30*.

Necropsy revealed that there was adequate normal renal tissue to sustain life and that death was due to the septicaemia, for which no original focus was found.

On *Day 17* the patient had become very deaf; thought to be due to vancomycin.

Case 7

A woman of 55 with chronic gall-bladder infection was treated by choledochotomy and cholecystectomy at another hospital; oliguria and paralytic ileus followed. Five days post-operatively, laparotomy revealed biliary peritonitis. Two days after this the patient was transferred to Hammersmith Hospital with renal failure.

Day 1: Oliguria, with blood urea 426 mg./100 ml. Temperature normal. *Day 2:* Dialysed on artificial kidney and blood urea reduced to 270 mg./100 ml. *Days 2–6:* Chloramphenicol and erythromycin for the biliary peritonitis. *Day 3:* Marked oedema. Patient collapsed and given a blood transfusion. *Day 6:* Right basal pneumonia, with temperature 100° F. (37.8° C.); cultures of sputum and from biliary drainage tube yielded *Staph. pyogenes* (+++, RRRSSS, 77). Blood urea rose to 380 mg./100 ml.

Days 6–13: Vancomycin given (total 12 g.). Over this period blood urea fell from 380 to 280 mg./100 ml. At first the temperature fell, but on *Day 8* again reached 100° F. (37.8° C.). On this day a perinephric abscess was drained—culture yielded *Ps. pyocyanea* (+++). From *Day 8–16* the temperature was swinging (up to 102° F.—38.9° C.), then subsided, and then rose again to 101° F. (38.3° C.). *Day 15:* Sputum culture yielded *Ps. pyocyanea*. Blood cultures were not taken, but clinically the patient had septicaemia. From *Day 13* the blood urea continued to fall and at *Day 22* was 194 mg./100 ml. *Days 15–21:* Polymyxin given, but patient failed to respond to treatment and she died on *Day 25*.

No information was available about any effect of the vancomycin treatment on hearing.

At necropsy *Staph. pyogenes* (now RRRRRS, still 77) was isolated from peritoneal fluid in paracolic gutter, from gastrostomy opening, and from septic infarcts in the lung. *Ps. pyocyanea* was isolated from sites deep to the right paramedian and flank incisions, from the bladder wall, and from the upper and lower parts of the peritoneal cavity.

Case 8

A man of 73 admitted with bilateral non-specific basal bronchopneumonia and a normal blood urea. The infection was treated first with penicillin and streptomycin, then with tetracycline, and then with chloramphenicol—each course lasting three to four days. During the first three days of the illness consolidation of the upper lobe of the left lung developed, with cavitation, but his temperature fell from 102° F. (38.9° C.) to subnormal. *Staph. pyogenes* (RRRSSS, 77) was isolated from sputum on *Days 5* (+), *13* (+++), and *15* (+++). There was retention of urine and increasing uraemia—the blood urea rose from 29 mg. per 100 ml. (*Day 3*) to 380 mg./100 ml. on *Day 13*.

Vancomycin was given (*Days 14–23*, total 7 g.), with dramatic clinical improvement, although specimens of sputa on *Days 19, 21*, and *23* still yielded small numbers of the same staphylococcus. The patient had a good uresis, and the blood urea fell to 68 mg./100 ml. (*Day 24*). *Day 23:* Erythromycin and chloramphenicol substituted for vancomycin; the temperature slowly rose and the blood urea, *Day 29*, was 235 mg./100 ml. He became disorientated, and died on *Day 32* in coma with renal failure.

The disorientation made assessment of his hearing difficult, but it was believed that he had become partly deaf. Necropsy was not performed, and the nature of the underlying disease was therefore not determined.

Case 9

A woman of 63 with carcinoma of the stomach was admitted as an emergency case, with a six-months history of persistent vomiting and loss of weight.

Days 2–14: Increasing pyrexia, rising to 103° F. (39.4° C.). Blood culture (*Day 12*) yielded *Staph. pyogenes* (RRRSSS, 53). *Day 14:* Subtotal gastrectomy. *Day 15:* Blood urea 16 mg./100 ml.

Days 14–21: Vancomycin given (total 12 g.). The infecting strain of *Staph. pyogenes* was again recovered from a blood culture and from a "polythene" intravenous transfusion catheter on *Day 16*. The blood urea rose to 66 mg./100 ml. (*Day 19*), but the temperature fell to and remained normal. *Day 21:* Vancomycin replaced by erythromycin and chloramphenicol. For six days the temperature remained normal, but the patient became jaundiced. *Days 27–34:* The temperature rose again, and blood culture, *Day 30*, was again positive. The blood urea rose continuously, and on *Day 46* reached 134 mg./100 ml. Throughout this period she received treatment with chloramphenicol, erythromycin, and novobiocin, either singly or in combination. She died with septicaemia on *Day 47*.

Necropsy was not performed. Severe nerve deafness was noted at the end of the course of vancomycin.

Response to Treatment

The results of treatment with vancomycin in these nine cases supports the view of Kirby and Divelbiss (1957) that it is valuable for use in hospitals in severe staphylococcal infections. All the patients were very ill—in each case the drug was used only as "a life-saving measure," and, except for Case 9, after the failure of previous chemotherapy.

Vancomycin was effective in saving the lives of five patients (Cases 1–5) (Table I). Patients 6 and 7 appeared

to have recovered from their staphylococcal infections with the aid of vancomycin, but succumbed to infection by *Ps. pyocyanea*, against which the drug is ineffective. Vancomycin is bactericidal for staphylococci *in vitro*, but it nevertheless failed to eliminate the organisms from four of these seven patients, although clinical cure of the staphylococcal infection was achieved. The chronic suppurative nature of the lesions in Cases 1, 2, and 3 presumably prevented the drug reaching all the organisms in adequate concentrations, and a proportion of viable bacteria therefore remained. Three of four patients with positive blood cultures (Table II, Cases 4, 5, and 6) were given an adequate course of treatment—in all three cases subsequent blood cultures were sterile.

The initial response of the infection to vancomycin of Cases 8 and 9 was good, but other antibiotics were substituted prematurely and the patients suffered a relapse and died. Had the course of vancomycin treatment been continued it is possible that a cure might have been effected where the bacteriostatic drugs were unavailing.

Toxic Effects of Treatment

Thrombophlebitis and gross loss of auditory acuity occurred with a number of the patients. One patient experienced brief hot flushes immediately after each dose of 0.5 g. of the drug in 20 ml. of saline. Some degree of thrombophlebitis eventually occurred with simple intravenous injections unless care was taken to use veins in rotation. No thrombosis occurred when vancomycin was given in 250-ml. saline infusions (over a 30-minute period) or by slow transfusion through a vena cava catheter.

Deafness was a serious sequel to treatment in Cases 4, 5, 6, and 9: it occurred either during or soon after treatment ended (Table III). Case 8 was also probably affected similarly, but the patient died before it could be confirmed. Cases 4, 5, 6, and 8 had variable degrees of renal failure with high blood urea levels at the time of vancomycin treatment. No. 7 also had a high blood urea level during treatment; but he died, and any effect the drug may have had on his hearing is not known. The other three patients had normal renal function and sustained no auditory damage. No subsequent improvement in hearing was noted in patients who were affected.

This clear indication of the danger of producing deafness in patients with renal failure suggests that the toxicity may be due to exceptionally high blood levels. If vancomycin is to be used for such patients then serial serum assays are essential to ensure that a maximum "safe" level is not exceeded, and to obtain an indication of the doses likely to maintain serum levels in the region of 10 μg./ml., which is an effective therapeutic concentration in most cases. The treatment of one such patient is described below, and the results of serum assays undertaken are shown in Table IV.

Control of Vancomycin Treatment in Patient with Renal Damage

An anuric patient with severe staphylococcal pneumonia after an emergency laparotomy was treated with vancomycin on failure of other chemotherapy and when he was apparently dying of his infection. When treatment began his blood urea was 270 mg./100 ml. Dosage was therefore controlled by serial serum assays. For each assay some eight dilutions of his serum, usually from 1 in 2.5 to 1 in 25, were made in fluid medium in 1-ml. volumes, using 6 by $\frac{1}{4}$-in. (15 by 2-cm.) tubes. Standard concentrations of vancomycin in human serum were diluted in the same medium. All tubes were then inoculated with 0.02 ml. of an overnight broth culture of *Staph. pyogenes*. The cultures were aerated on a Kahn shaker in a room at 37° C. It was found possible to read the end-points of inhibition of growth after four to five hours and so be able to adjust the next dose. Assay results calculated from readings made at the end of 18 hours' incubation were not materially different.

The initial dose of vancomycin administered was only 500 mg., and subsequent doses (250 or 500 mg.) were given or omitted according to the results of the assays. Daily variations in dosage and the number of assays undertaken are shown in Table IV. The total drug given over 11 days was only 5.125 g. Serum vancomycin levels lay between 3.3 and 20 μg./ml., except after the initial dose: 24 of the 32 levels were between 5 and 12 μg./ml. On this regime the pneumonia subsided, his condition greatly improved, and the blood urea fell to 102 mg./100 ml. over the 11 days. The assay results indicated the need, therefore, to increase the dose as renal function improved. Several sputum cultures were made—all were free from *Staph. pyogenes*. The patient, however, also had a retroperitoneal infection with the same strain of staphylococcus, and continued to discharge the pus through his abdominal operation wound. This did not apparently delay his recovery from the pneumonia. During treatment, and in the month following, no impairment of hearing was detected. However, a month after the first course he was given a second, assay-controlled, course for the retroperitoneal infection. Some time after the second course ended he suffered some loss of auditory acuity in the upper wavelengths, although during treatment the blood urea was not raised.

Serum vancomycin assays are now undertaken routinely with patients having a raised blood urea, and audiometric tests are made before, during, and periodically after treatment for as long as they remain in hospital.

Discussion

The response of patients in this series to vancomycin therapy confirms that the drug is an effective weapon. It would seem that acquired resistance is unlikely to be a problem, and natural resistance to the antibiotic occurs with few strains. All strains of *Staph. pyogenes* isolated from routine bacteriological specimens and nasal swabs from patients and nurses in Hammersmith Hospital for 13 months from the beginning of 1958 have been tested by a ditch-plate technique for their sensitivity to vancomycin and no resistant strains have been found.

Because the drug must be given intravenously and because of its toxicity to the eighth nerve, it should be used mainly for severe staphylococcal infections when other chemotherapy is ineffective either because of the resistance of the infecting strain or for other causes. The drug is bactericidal and therefore especially valuable for patients particularly prone to infection or whose own defences are impaired.

Failure of treatment, and the death of four patients in this series were due neither to resistance of the organism to the drug nor to undue delay before change of treatment to vancomycin was made. Two of the patients (Cases 6 and 7, Table III) recovered from the staphylococcal infection but died of *Ps. pyocyanea* septicaemia. The other two (Cases 8 and 9) improved while on vancomycin, but after six days' treatment in each case the drug was prematurely withdrawn and bacteriostatic chemotherapy was substituted. Thereafter the patients' condition deteriorated and they died. Failure to eliminate the infecting strains of staphylococci in a number of cases, even where clinical

recovery was achieved, underlines the need to give an adequate course of the drug.

Our experience with patients with high blood urea levels shows that a check of blood vancomycin levels must be kept if deafness is to be avoided, although fewer assays might be required than were undertaken for the case described above.

The nine patients in this series were all treated with vancomycin in a nine-months period from the beginning of November, 1957. Dosage had seemed fairly conservative, for no patient received more than 1–2 g. a day and no patient with renal failure more than 13 g. in all. At that time the danger of deafness in patients with high blood levels—that is, with impaired renal function—was not appreciated by us and routine serum vancomycin assays were not undertaken. Subsequently Geraci *et al.* (1958) reported moderate degrees of perceptive deafness without labyrinthine disorder in one of a series of six patients and in one other patient. One had normal renal function and the other blood urea levels of 60–100 mg./100 ml.—in both patients serum vancomycin levels were very high (80–95 μg./ml.). In clinical studies two years earlier the same workers encountered no auditory impairment (Geraci *et al.*, 1956). Kirby and Divelbiss (1957) did not note any loss of hearing in two patients with impaired renal function. One was treated with 2 g. of vancomycin a day for eight days and had consistent 24-hour blood levels of 20–32 μg./ml.; the other, on 4 g. a day, had 12-hour levels of 100 μg./ml. on three occasions.

Geraci *et al.* (1958) noted a number of other toxic effects, including skin rashes of various types, fever, and chills. They detected no toxic effects on the kidneys, liver, or haemopoietic system. They found that the average serum vancomycin levels in normal subjects given 2 g. of the drug a day in divided doses was 13 μg./ml. and that damage to the eighth nerve did not result with such levels. Such levels should be adequate in treating staphylococcal infections, for nearly all strains tested by a number of workers have been sensitive to 2.5 μg. of vancomycin per ml. or less.

Kirby and Divelbiss (1957) found that when patients with normal renal function were given 1 g. of vancomycin 12-hourly or 0.5 g. six-hourly the serum levels 12 hours after each dose were mainly of the order of 3–10 μg./ml.; after two to three days' treatment a cumulative action was noted. We found similar levels in two patients treated with the drug since the series described in this paper. Further experiments are required to determine levels which can be maintained without adverse sequelae. Toxic effects are easier to avoid when the drug is administered by continuous drip transfusion. The concentration of the drug in the serum varies slowly when it is given by this method and therefore few serum assays are needed. Moreover, closer and more rapid control of the serum level can be achieved by altering the concentration of vancomycin in the transfusion fluid.

Summary

The treatment by intravenous vancomycin of nine patients with severe staphylococcal infections is described; of these, only three had normal renal function. The infecting strains of *Staph. pyogenes* were all resistant to several antibiotics, and treatment with other antibiotics had failed. Vancomycin therapy led to a good clinical response. Two of the patients died when vancomycin was withdrawn before the infection was controlled. Two others recovered from the staphylococcal infection but died subsequently of *Ps. pyocyanea* septicaemia.

Although vancomycin is bactericidal *in vitro*, three of the five surviving patients continued to harbour the infecting staphylococcus in lesions.

The danger of drug deafness in uraemic patients is stressed. This may occur during or after treatment. Several uraemic patients developed toxic deafness on dosage of 1–2 g. daily, although none received more than 13 g. in the course. A regime of lower doses controlled by "rapid" serum assays is outlined, and was used successfully in the management of a uraemic patient with staphylococcal pneumonia. The total amount given was only 5.125 g. over 11 days.

Thrombophlebitis occurred in some patients when the vancomycin was given by simple intravenous injection in 10 ml. of saline, but not when it was administered in 250-ml. infusions over a 30-minute period or in larger volumes in saline or 5% glucose transfusions.

The drug must be given intravenously, and as it is also toxic to the eighth nerve it is likely to be used mainly in hospital for severe staphylococcal infections, especially where this organism is resistant to several other antibiotics or where other chemotherapy is otherwise unavailing. It is also valuable when a bactericidal drug is particularly desirable—that is, staphylococcal infections in patients whose normal defence mechanisms are defective.

We thank the physicians and surgeons in charge of the reported cases for their co-operation; Mr. V. J. Briffa, of the department of surgery, for undertaking the audiometric tests; and Messrs. Eli Lilly, who supplied the vancomycin for trial. We are particularly grateful to Dr. Mary Barber for a great deal of help and advice, and to Mr. A. Medway, who carried out the bacteriophage typing of the infecting strains of staphylococci.

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The Education Advisory Committee of the Universities Federation for Animal Welfare has protested to the United States Ambassador about the action of the National Science Teachers Association, Washington, in awarding a prize in their "1958 Science Teacher Recognition Program" to a biology teacher in Buffalo, New York, who has encouraged his high school pupils to carry out experiments on live animals. According to U.F.A.W., the experiments done with and by the children include "forcing into the lungs pepper and other dusts and smoke of such density as to provoke violent shutting of the glottis; toxicity tests to find what dose of inhaled nicotine will kill 50% of treated animals; perfusion with amateur apparatus devised by a schoolgirl; weekly routine transfers of cancer cells peritoneally; and the production in live animals of metastases, especially in the lungs."

OCCURRENCE OF TETANUS SPORES IN MATERIALS USED FOR DRESSING WOUNDS

REPORT OF THE PUBLIC HEALTH LABORATORY SERVICE (MEDICAL RESEARCH COUNCIL, LONDON)*

The present investigation was prompted by the occurrence in the North Staffordshire Royal Infirmary of five post-operative cases of tetanus within a fortnight. This is not the place in which to describe the outbreak itself (see Report, 1958). Suffice it to say that, in searching for the cause, suspicion was thrown, among other possible sources, upon the dressings.

Reported Occurrence of Tetanus Spores in Various Substances used for Therapeutic Purposes

Before describing our own investigations it may be helpful to make a brief résumé of the findings of previous workers.

Catgut

In the past numerous cases of post-operative tetanus occurred owing to the use of contaminated catgut. The problems of infection and of sterilization presented by this substance have been ably discussed by Bulloch, Lampitt, and Bushill (1929), Mackie, McLachlan, and Anderson (1929), Porteous (1934), and Dalrymple-Champneys (1936), and we do not propose to deal with them. Catgut is now effectively sterilized, and it is many years since it was responsible for a case of tetanus in this country.

Gelatin

Gelatin is made by treatment of hides and bones with lime and hydrochloric acid, and extraction of the gelatinous mass with water at 60–80° C. The commercial product is not infrequently contaminated with tetanus spores. Tuck (1904) demonstrated their presence in 6 out of 15 samples examined. Gelatin was at one time used as a haemostatic agent, and as such was responsible for occasional cases of tetanus (Smith, 1908).

Glue—Bunion Pads

In the United States of America, Armstrong (1925) recorded 11 cases—9 of them fatal—of tetanus following the use of bunion pads as a dressing for vaccination wounds. Bunion pads consist of a felt ring coated on one side with a film of glue. Of about 200 pads examined by Bengtson (see Armstrong, 1925), 25% were found to contain toxigenic tetanus spores. The glue prevents air from reaching the wound, thus leading to the establishment of anaerobic conditions. Tetanus spores are then able to germinate and multiply in the necrotic tissue resulting from growth of the vaccinia virus.

Court Plaster

In the days of the open-blade razor court plaster was in frequent demand for dressing cuts caused during shaving. Occasional cases of tetanus followed its use. McCoy, Leake, and Corbitt (1917) found tetanus spores in 3 out of 14 specimens examined. These authors were of the opinion that the plaster left the manufacturer free from tetanus spores and that it became contaminated later, but the evidence was not conclusive.

Powder

Various powders—talc, starch, and fuller's earth—come directly or indirectly into contact with wounds. All of them in their natural state are contaminated with earth, and often with human or animal excreta, and contain large numbers of aerobic and anaerobic spore-bearing organisms.

Zweifel (1910) described four cases of neonatal tetanus following the use of bandages dusted with *Bolus alba* for dressing the umbilical stump. Normally the powder was sterilized by dry heat in large pans at 170–200° C. for several hours. This method was very effective, for 10,000 babies had been dressed with powder treated in this way without mishap. It was not till the midwives by mistake failed to sterilize the powder that cases of tetanus occurred.

Another dusting-powder that has been associated with neonatal tetanus is fuller's earth. Dr. Wynn Westcott, the coroner for North-east London, said that he held inquests on about four cases of tetanus every year in infants whose navel and buttocks had been dusted with this substance (Report, 1908). Fuller's earth is a porous aluminium silicate containing some iron, which doubtless promotes the establishment of anaerobic conditions. It used to be quarried near Reigate.

There are numerous records of the finding of tetanus spores in talcum powder. In a thesis for a doctor's degree at Nancy, of which unfortunately we have been able to see only an abstract, Durand (1919) reported the cultivation of pyogenic bacteria and of tetanus spores from simple and compounded powders used on wounds and irritated surfaces. In New Zealand, Tremewan (1946) encountered four cases of neonatal tetanus in which infection of the umbilical stump had occurred through talc dusting-powder. Hills (1946), who examined the baby powder, isolated tetanus bacilli from it. Inquiry revealed that the talc had been imported from India in unlined jute sacks and had not been sterilized. Magnesium silicate is found as a natural deposit and is produced commercially as talc, soapstone, French chalk, or steatite. The finer grades are sold as talc. In India, where it is quarried, the mineral becomes heavily contaminated with human and bovine excreta. According to the *British Pharmaceutical Codex* talcum purificatum is talc that has been boiled with dilute hydrochloric acid and subsequently washed and dried at 110° C. In Queensland, Johnson (1956) collected records of 10 cases of post-operative tetanus during the years 1948–54. In one of them tetanus bacilli were grown from the powder used for the rubber gloves. Sevitt (1949), in this country, also reported the finding of tetanus spores in talcum powder, both before and after sterilization. He was of the opinion that the sterilized powder had become recontaminated from dust.

Welch, Slocum, and Herwick (1942), in the United States of America, found that about 50% of sulphonamide dusting-powders on the market contained aerobic and anaerobic spore-bearing organisms. Tetanus spores were not demonstrated, but washed tetanus spores introduced into the subcutaneous tissues of the

*The following bacteriologists took part in the inquiry: Dr. B. R. Sandiford (Birmingham), Dr. J. E. Jameson (Brighton), Dr. C. E. D. Taylor (Colindale), Dr. B. Moore (Exeter), Dr. G. B. Ludlam (Leeds), Dr. N. S. Mair (Leicester), Professor D. T. Robinson (Liverpool), Dr. A. R. Blowers (Middlesbrough), Dr. D. J. H. Payne (Northallerton), Dr. K. E. A. Hughes (Portsmouth), Dr. A. C. Jones (Shrewsbury), Dr. E. M. Mackay-Scollay (Stafford), Dr. P. B. Crone (Sunderland), and Dr. J. A. Boycott (Taunton).

guinea-pig were apparently activated by the simultaneous introduction of sulphonamide powder.

Vaccines

Tetanus has followed the administration of both smallpox and bacterial vaccines (Smith, 1908). Carini (1904) demonstrated the occasional presence of tetanus spores in vaccine lymph. Lymph, however, never gives rise to tetanus unless the vaccination site is rendered anaerobic by an occlusive dressing.

In 1902, at Mulkowal in India, 19 out of 107 persons inoculated with Haffkine's plague vaccine died of tetanus, owing apparently to contamination of one of the bottles (Report, 1907).

Antisera

In 1902 there was an outbreak of tetanus in St. Louis, Missouri, following the use of diphtheria antitoxin. The horse yielding the serum was shown to have been in the incubation period of tetanus (Smith, 1908).

Cellulose Wadding

In 1929 Fildes drew attention to the fairly high incidence of tetanus after hysterectomy. In 1935 he demonstrated the presence of tetanus spores in dressings made of cellulose wadding, and described two cases of tetanus developing in orthopaedic practice from splints packed with this material (see Pulvertaft, 1937). Pulvertaft (1937), investigating a fatal case following hysterectomy, was likewise able to demonstrate the presence of tetanus spores in cellulose wadding. This substance, in the form of sanitary pads, had been applied unsterilized to the vulva before operation. Examining sanitary pads of different origin, he found that all of them contained spores of *Clostridium tetani, Cl. welchii,* and *Cl. sporogenes* either alone or in combination. Pulvertaft investigated the method of manufacture of cellulose wadding from soft woods—mainly red spruce and pine—and concluded that the heat and chemical treatment used were sufficient to destroy all spores. The contamination of the wadding must therefore occur later.

Pulvertaft's findings were confirmed by Goodhart and McIntosh (1941), who examined a sample of the treated wood pulp used for the preparation of cellulose wadding and cultivated tetanus bacilli from it.

Cotton-wool

Brown, grey, or unbleached cotton-wool is wool that has not been subjected to any chemical treatment since it left the field on which the cotton was grown. According to the description given in the Report (1941) of the Tetanus Committee of the Royal College of Obstetricians and Gynaecologists, in the manufacture of white wool the grey product is boiled with a strong alkali and bleached with an oxidizing agent. It is then sterile, but it is apt to be recontaminated to a greater or less extent during the drying process, in which large volumes of hot air are blown over it. The air is contaminated with dust from the crude cotton-wool, and the wool filters off the organisms contained in it. Since the war the processing of cotton-wool has been improved, and steps are now taken as a rule to prevent recontamination during the final stage of drying.

Pulvertaft (1937) found tetanus spores in an accouchement set prepared with brown and white cotton-wool; and Goodhart and McIntosh (1941) were able to cultivate tetanus bacilli from the only sample of brown cotton-wool they examined, but not from any of three samples of white cotton-wool, though these three samples did contain aerobic and anaerobic spore-bearing organisms. Cane (1938) described a case of tetanus in a man who had a pressure sore over a kyphotic spine. The splint over the spine had been padded with unsterilized brown wool. A similar case was reported earlier by Sternberg (1931) in a boy who developed an abscess under a plaster splint after an operation for tuberculosis of the hip-joint. The tetanus spores that were found in the pus were apparently derived from the brown wool that had been put under the splint at the time of the operation and had come into contact with the fistula of the abscess. Johnson (1956), in Queensland, reporting on seven cases of neonatal tetanus, observed that in one of them tetanus bacilli were isolated from an imperfectly sterilized umbilical pad similar to those applied to the infant.

So far as these few observations go, brown wool would appear to be more likely to convey tetanus than white. Whether this is because it is more heavily contaminated with spores, which is probable, or because it is less often sterilized before use, which is also probable, it is impossible to say.

Plaster-of-Paris Bandages

Murray and Denton (1949), in Montreal, described a fatal case of tetanus in a patient who had been operated on for a tuberculous knee-joint and whose leg had been set in plaster. The onset of tetanus was delayed for nearly a month. Tetanus bacilli were isolated from the wound and also from plaster bandages of the same make as those used for the case. An examination of 28 further plaster bandages revealed the presence of *Cl. welchii* in 24 of them, as well as other spore-bearing bacilli. Greenberg (1949), who examined 163 plaster-of-Paris bandages, found 111 (68%) to contain spore-bearing anaerobes, *Cl. welchii* being much the commonest.

Tetanus Spores in Dust and in Wall-plaster

The original observations of Nicolaier (1884) on the presence of tetanus spores in earth and dust have been confirmed many times; and numerous workers have demonstrated their occurrence in the faeces of man and domestic animals. That dust in the operating theatre may likewise contain tetanus spores was shown by Robinson, McLeod, and Downie (1946), who isolated the organisms from the dust on the floor, the wall, and the blades of a fan in one theatre in which a patient had developed tetanus after a pneumothorax operation, and from the dust of another theatre in which a patient had developed tetanus after an operation for piles. The first theatre adjoined a field, the earth of which was shown to contain tetanus spores. Sevitt (1949), who likewise found tetanus spores in the dust of a theatre in which two post-operative cases of tetanus had occurred, was of the opinion that they were derived from the plaster-hair mixture that had been used for repairing the ceiling. Contaminated theatre dust may perhaps have been responsible for the case of tetanus described by Wright (1930) in a patient who developed a pulmonary infarct after a partial gastrectomy. No tetanus bacilli were found in the operation wound or in the jejunal contents, but they were present in the infarcted area of the lung. More recently, Lowbury and Lilly (1958) reported the isolation of tetanus bacilli from 33 out of 50 samples of air from an operating

theatre. No clinical case, however, of tetanus had occurred during the previous nine years, indicating that the risk of infection of the patients from this source must have been very small. On the other hand, Johnson (1956), in Queensland, recorded a case of tetanus in which spores of the bacillus were demonstrated in the dust of the operating theatre.

Description of the Present Investigation

The investigation was carried out between May, 1957, and June, 1958, by 14 public health laboratories situated in different parts of England. Dressings of various kinds, as supplied by the manufacturer or agent, were provided by the local hospital management committees. No arrangement was made for each laboratory to examine the same number of samples of any given material, or for equal numbers of samples to be taken from different manufacturers. The selection was haphazard, the main purpose of the investigation being not so much to estimate the comparative risk of using different materials as to find out whether there was any risk at all. The inquiry was in fact more qualitative than quantitative.

No standard technique was laid down, but the following notes were issued for general guidance.

Cotton-wool.—The manufacturer's package is opened by cutting along the whole length of the immediate paper pack with a sterile razor or scalpel. The cotton-wool roll is shelled out on to sterile greaseproof paper and unwound for a distance of one circumference. Beyond this, at convenient sampling distances, three strips of wool 1 in. (2.5 cm.) wide are cut with sterile scissors, across the full breadth of the roll. The strips are placed in 2-lb. (0.9-kg.) Kilner preserving jars containing 500 ml. of nutrient broth to which are added three pieces of sterile sheet iron about 1 sq. in. (6.5 sq. cm.) each. The lid of the jar is loosely secured, and the jar is placed in a bath of hot water, which is brought to the boil and maintained at boiling point for five minutes. The jar is then removed, its lid tightly secured, allowed to cool, and incubated at 37° C. The main purpose of the heating is to drive off oxygen from the broth and to destroy vegetative aerobic organisms which may, like *Proteus*, interfere with the subsequent isolation of the tetanus bacillus in pure culture. Some workers may prefer to pour boiling nutrient broth on to the cotton-wool and incubate without further heating.

Gauze, lint, tulle gras, and similar materials may be sampled along similar lines.

Dusting Powders.—3-g. and 1-g. amounts are sown into 15 ml. of Robertson's cooked meat broth contained in screw-cap Universal containers. The container is put into boiling water for five minutes before incubation.

Isolation of Cl. tetani from Primary Cultures

Examination of the primary growth in Universal containers may be made after five days' incubation and in Kilner jars after seven days' incubation. Microscopical examination of primary cultures provides a fairly accurate forecast on the outcome of subculture. Methylene blue, alone or combined with carbol-fuchsin, is a satisfactory stain to use.

Though the mature spore is spherical and terminal, it should be remembered that in the early stages of development the spore may be oval or even irregular in shape. Different strains of tetanus bacilli, moreover, vary greatly in the ease with which they form spores; with occasional strains spores may not be detected in culture for 8 to 10 days.

Subculture

Plates.—A single horse-blood or Lemco-agar plate which has been well dried in the incubator at 37° C. is inoculated over approximately half its surface. As an alternative to drying, the agar (Davis) concentration may be increased up to 4%.

Slopes.—Freshly prepared horse-blood agar (Davis 1.5%) and Lemco agar are sloped in 6 by 5/8-in. (15 by 1.6-cm.) tubes to a level about three-quarters of the way up the tube. One slope of each medium is inoculated by a Pasteur pipette with about 0.2 ml. of primary culture. The inoculation should be made into the condensation fluid, care being taken to avoid contamination of the slope proper on introducing or withdrawing the pipette. Anaerobic incubation should be for between 20 and 30 hours.

On slope culture the wispy, thread-like margin of growth chased by the smoother "salad oil" droplets which have derived from a thin moist film below is typical of a positive *Cl. tetani* culture. A similar picture is afforded by plate culture, given the right conditions of surface moisture. A faint haemolysis is apparent on blood plates.

Fildes (1925a) himself recommends that before inoculation the slope should be kept at room temperature till the apex is dry. On such a slope after 24 hours' incubation the apex is covered by extremely fine ascending filaments of growth, roughly parallel or recurved and tangled, spreading upwards almost on to the bare glass.

Pure cultures from the marginal growth are readily obtained on subculture into cooked meat broth, but the tetanus threads are short-lived under atmospheric conditions and should be subcultured as soon as possible after the tubes have been removed from the anaerobic jar. To obtain the tetanus bacillus in pure culture, alternate inoculation of tubes of cooked meat medium and agar slopes may be necessary.

Very rarely strains of the tetanus bacillus are met with which are non-motile and do not give rise to the typical filmy growth on solid media. Isolation of these organisms has to be carried out by the ordinary surface-plating method.

Identification

The simplest confirmatory tests to apply to a pure culture are agglutination for specific identity, and the inoculation of animals for the demonstration of toxicity.

For agglutination an O antiserum should be used, as this acts on a common group antigen. H antisera are type-specific and unsuitable for simple confirmation of the species. An O antiserum acts on both toxic and non-toxic strains, and will thus lead to the identification of strains that do not give rise to tetanus in experimental animals.

For animal toxicity tests 1 ml. of a 48-hour cooked meat broth culture should be inoculated into the thigh of a guinea-pig. Typical signs of ascending tetanus will develop in about 30 hours. In cases of doubt, a control animal protected by the previous inoculation of tetanus antitoxin may be used in addition.

Mice are slightly less susceptible to tetanus toxin than guinea-pigs, but may be used instead if more convenient.

Results

The results are given in Table I and in summarized form in Table II.

It will be seen that with three exceptions all the isolations of tetanus bacilli were made from cotton-wool or cotton-wool bandages. Moreover, of the 222 samples of cotton-wool examined, all but one of the positive samples were of the unbleached variety. It will be further noticed from Table I that a much higher proportion of samples were found by the Stafford laboratory to contain tetanus spores than by any other laboratory. The reason for this was apparently not that any special technique was used in the Stafford laboratory, but that this laboratory received cotton-wool

TABLE I.—*Numbers of Hospital Dressings Examined for* Cl. tetani *with Results*

Type of Dressing	Birmingham	Colindale	Exeter	Leeds	Leicester	Liverpool	Middlesbrough	Northallerton	Norwich	Plymouth	Portsmouth	Salisbury	Shrewsbury	Stafford	Sunderland	Taunton	Total
Cotton-wool: Bleached			4 (1)	19		3	12	21	12	1	13		3	10	4	20	122 (1)
Cotton-wool: Unbleached	2 (1)	4 (1)	2	4	9	1	3	4	2	2	4	2 (2)	4 (3)	21 (9)		8	72 (16)
Bandages									2		1		5	8 (4)		12	28 (4)
Cellulose wadding			3	4		2		15	1	1	2			10	1	6	45
Wadding bandages									2				4				6
Gauze: Paraffin						1			10					4			15
Gauze: Swabs, ribbon, roll			8 (1)	33		16	1	11	15	3	27		2	23	6		145 (1)
Gauze: Plaster-of-Paris bandages and gypsum				3		1	1		8		1			7			21
Cotton and crepe bandages			3	26		50		5	5	1	8		4		2	4	108
Stockinet				1		1			1				2	2 (1)	1	4	12 (1)
Lint			2	6		1	1	7	3		3			2	2		27
Gamgee								8		1	7			1			17
Felt				3										1	1	6	11
Talc or other dusting-powder						1	1		13					1	1		17
Tow				1		1		10	1		2				1	4	20
Total	2 (1)	4 (1)	22 (2)	100	9	78	19	81	75	9	68	2 (2)	24 (3)	90 (14)	19	64	666 (23)

Figures in parentheses indicate positive results.

from one particular firm whose products, which were heavily contaminated, were not used in the other areas studied. When samples of this firm's products were sent to other laboratories, tetanus bacilli were found as at Stafford. Too few samples of many of the materials listed in the tables were examined to justify any conclusions being drawn, but in view of Pulvertaft's findings it is rather surprising that none of the 51

TABLE II.—*Summary of Results in Table I*

Type of Dressing	No. of Samples Examined	No. Found to Contain Tetanus Spores	Percentage Containing Tetanus Spores
Cotton-wool: Bleached	122	1	0·8
Cotton-wool: Unbleached	100	20	20·0
Cellulose wadding	51	0	0
Gauze: Paraffin	15	0	0
Gauze: Swabs, ribbon, roll	145	1	0·7
Gauze: Plaster-of-Paris bandages and gypsum	21	0	0
Cotton and crepe bandages	108	0	0
Stockinet	12	1	8
Lint, gamgee, felt, and tow	75	0	0
Dusting powder	17	0	0
Total	666	23	

samples of cellulose wadding and bandages proved to contain tetanus bacilli. It is, of course, possible that the organisms were there but were not isolated, or that the wadding had been treated chemically so as to destroy them. With two exceptions (strains that were discarded prematurely by mistake) every strain recorded in Table I was shown to be toxic to the guinea-pig or the mouse. Both Fildes (1925b) and Kerrin (1929), however, found that a considerable proportion of tetanus strains isolated by them were non-toxic. In Fildes's series no fewer than 20 out of 75 strains fell into this category. Kerrin found that the non-toxic strains he tested produced just as active a haemolysin as the toxic strains, even though they were unable to kill animals.

Discussion

These results need little comment. It seems clear that unbleached cotton-wool is the most frequently contaminated form of dressing. From the practical point of view all dressings that are liable to come into contact with a wound or broken surface should be sterilized. Is this, however, sufficient? The more radical course would be to ensure that no unsterilized dressings were allowed into the theatre block. Otherwise tetanus spores may be liberated and gain access to wounds either directly or indirectly. If this conclusion is accepted, it follows that dressings should not be sterilized in the theatre.

Other precautions should, of course, be taken to prevent tetanus spores being carried into the theatre on shoes contaminated with street dust (see Gilles, 1937; Ostertag, 1942), by contaminated air (see Lowbury and Lilly, 1958), or by other means, or liberated into the air of the theatre from defective plaster. During the course of the present investigation carried out by the Public Health Laboratory Service tetanus bacilli were demonstrated on the fan and in the air intake duct of one theatre as well as in the wall plaster of the theatre sterilizing-room.

Tetanus spores are unable to germinate in healthy tissue. Could they do so, tetanus would probably be a frequent post-operative complication, as they must often be deposited in the wound from contaminated air. In order to germinate they must be implanted either in dead tissue or in some inanimate material in contact with the wound, such as gauze or cellulose wadding (see Pulvertaft, 1937), in which anaerobic conditions may develop; or they must be accompanied by certain organisms that are able to lower the oxidation-reduction potential of the tissues, such as *Cl. welchii* (Tulloch, 1919).

These considerations point to contaminated dressings as being a source—and possibly an important source—of post-operative tetanus. To minimize this danger dressings should be sterilized before they are taken into the theatre suite, and should be protected from recontamination from air or dust in the theatre.

The materials examined in our investigation did not include rubber gloves used in the operating theatre or ward. Considering that gloves are dusted with potentially contaminated powder, are by no means always properly sterilized, and come into close contact with the wound, they may well present as great a danger as dressings.

Summary and Conclusions

A brief review is given of the various materials used in treatment that have been responsible in the past for conveying tetanus.

In the present investigation 666 samples of various forms of dressing materials were examined for tetanus bacilli by 14 public health laboratories situated in different parts of England.

Tetanus bacilli were isolated from 23 samples. Of these, all but three were of unbleached cotton-wool or cotton-wool bandages, most of them coming from a single firm.

These results suggest that contaminated dressings are a possible source of post-operative tetanus. Contaminated gloves may be of equal or greater danger, but no observations were made on them.

It is concluded that every attempt should be made to prevent tetanus spores being carried into the theatre by air, street dust, dressings, or in other ways.

All dressings should be sterilized before being taken into the theatre suite, and not in the theatre suite itself.

We thank all members of the regional hospital boards and hospital management committees who provided the necessary samples for examination.

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RED-CELL APLASIA AND BENIGN THYMOMA

STUDIES ON A CASE RESPONDING TO PREDNISONE

BY

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In 1928 Matras and Priesel described aplastic anaemia associated with a thymic tumour. Since then reports of 16 similar cases have been published (see Soutter *et al.*, 1957). The bone-marrow aplasia has usually been shown to affect the red-cell series only, although pancytopenia has also been described.

We report the case of a patient with pure red-cell aplasia and a benign thymic tumour in whom thymectomy had no effect on the anaemia. Subsequently, prednisone therapy was followed by the restoration of normal erythropoiesis. An attempt to demonstrate the presence of an inhibitor of erythropoiesis in the patient's plasma was unsuccessful.

Case Report

The patient was a widow aged 71. At the age of 58 she had angina of effort, and, as she was said to be anaemic, was treated with an oral liver preparation for a few months. Subsequently she had slight effort dyspnoea, which increased after an attack of "influenza" in November, 1956. She was then treated with injections of liver for five months without benefit. At no stage were there any symptoms suggestive of myasthenia gravis, nor had she taken any marrow-depressant drugs.

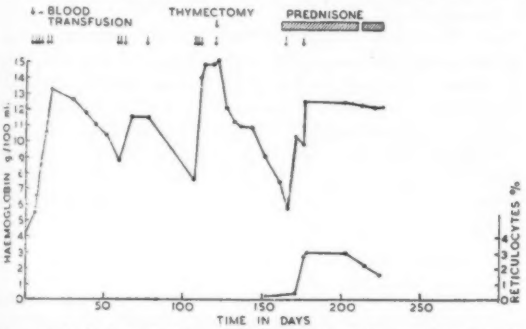
She was admitted to Cardiff Royal Infirmary on July 17, 1957, when she was found to have profound anaemia and senile purpura. Blood examination on admission gave the following results: Haemoglobin, 4.3 g./100 ml. (29%); R.B.C., 1,300,000/c.mm.; P.C.V., 14%; M.C.H.C., 31%; M.C.V., 107 cubic microns; reticulocytes, 0.2% (2,600/c.mm.); W.B.C., 7,300/c.mm. (normal differential); platelets, 276,000/c.mm. After an intravenous injection of Fe-59 the plasma half-clearance time was found to be 300 minutes (normal 70–120 minutes) and the iron utilization nil up to 18 days. The mean survival of normal red cells in the patient's circulation was 91 days. The direct anti-human-globulin test was negative; serum iron, 260 μg./100 ml.; and serum vitamin B_{12}, 306 $\mu\mu$g./100 ml. Serum proteins measured 6.1 g./100 ml. (albumin 3.6 g., globulin 2.5 g.); serum bilirubin, 0.4 mg./100 ml.; alkaline phosphatase, 9.7 K-A units; thymol turbidity, 2 units; and blood urea, 24 mg./100 ml. Wassermann reaction and Kahn test were negative. A histamine test meal showed free acid. Amino-acid chromatography of the urine was within normal limits. Iliac crest puncture revealed an almost complete absence of red-cell precursors; leucocyte and platelet formation appeared normal. A chest *x*-ray film showed a rounded opacity in the lower part of the right anterior mediastinum. The radiological appearances were suggestive of a thymoma.

For four months the patient was treated by repeated blood transfusions; the haemoglobin fell at a rate of approximately 1% a day between transfusions, as shown in the Chart, but leucocyte and platelet counts were normal throughout. Reticulocytes were never seen except shortly after transfusion. On November 13 the anterior mediastinal tumour was removed by Mr. D. M. E. Thomas; it was encapsulated, was 10 cm. in diameter, and histological examination (Dr. R. M. E. Seal) showed that it was a benign thymoma. The marrow from a rib removed at

operation was of less than average cellularity and contained practically no erythropoietic tissue.

The patient's post-operative course was uneventful, but her haemoglobin continued to fall at the pre-operative rate; no reticulocytes were seen on repeated examination and further blood transfusion was necessary.

Six weeks after operation, treatment with prednisone, 60 mg. daily, was started. During the next 15 days the reticulocyte count rose to 116,000/c.mm. (see Chart). At this time the haemoglobin was 12.5 g./100 ml. (84%) and it remained above 12 g./100 ml. for the rest of her life; no further transfusions were needed. On the forty-second day of prednisone treatment the bone marrow showed active normoblastic erythropoiesis with a myeloid: erythroid ratio of 3:1. Prednisone was then gradually withdrawn without any significant fall in haemoglobin or reticulocyte count during the subsequent 20 days. Towards the end of this period the patient developed staphylococcal septicaemia and died, despite intensive chemotherapy.



Haematological and therapeutic data in patient with red-cell aplasia and benign thymoma.

Post-mortem examination revealed an abscess over the sacrum and multiple metastatic staphylococcal lesions. Red marrow filled the sternum and about three-quarters of the proximal part of the femur. Sections of ribs and femur showed normal haemopoietic marrow with numerous red-cell precursors.

Animal Experiments

Because of the reported association between thymic tumours and red-cell aplasia an attempt was made to demonstrate a humoral factor in the plasma of our patient, capable of depressing red-cell production in experimental animals.

Materials and Method

The animals used were female Wistar rats weighing 200–350 g. They were anaesthetized and 2 ml. of heparinized plasma was injected intravenously by direct cannulation of one jugular vein. Twenty-four hours later the opposite jugular vein was cannulated and a further 2 ml. of plasma injected, followed by 1 ml. of a buffered sodium citrate solution containing approximately 1 μc of radioactive iron (Fe-59). After a further 24 hours blood was obtained by cardiac puncture and the animal was destroyed. At the beginning and end of each experiment a specimen of blood was obtained from the tail, and the haemoglobin, P.C.V., and reticulocyte count were determined.

The radioactivity of the heparinized cardiac blood was determined by direct γ-counting in a well-type scintillation counter, and the percentage of injected iron utilized for haemoglobin synthesis was calculated in the following way:

$$\%\ \text{utilization Fe-59} = \frac{\text{activity in counts/sec./ml. blood} \times \text{blood vol.} \times 100}{\text{total activity injected in counts/sec.}}$$

Belcher *et al.* (1954), using "August" rats, found the blood volume to be equivalent to 5.3 ml./100 g. weight, and for the purposes of our calculations this figure was assumed to apply to our animals.

Three identical experiments were carried out as follows, using four animals on each occasion:

Experiment 1.—With patient's plasma, obtained before thymectomy and while no treatment other than blood transfusion was being given. All the animals survived.

Experiment 2.—With patient's plasma, post-operatively and after prednisone had been given. Two of the animals died.

Experiment 3.—With pooled normal human plasma. One animal died and one deteriorated so much that the second injection of plasma was not given.

Results

The iron-utilization figures, as a percentage of the injected dose of Fe-59 for each experiment, are as follows:

	Experiment 1	Experiment 2	Experiment 3
Rat 1 ..	31%	40%	39%
,, 2 ..	42%	42%	29%
,, 3 ..	38%	—	—
,, 4 ..	35%	—	—

Although there were variations in the haemoglobin and reticulocyte counts during these experiments, the figures above show that the effect of the patient's plasma obtained before treatment on erythropoietic activity in the rats was not significantly different from that of normal plasma or from the patient's own plasma obtained after treatment. The percentage utilization of iron for haemoglobin synthesis in each case was of the same order as that found by Lamerton *et al.* (1956) in normal August rats.

The method of investigation employed in this study has its limitations, and we can only say that no humoral factor was demonstrated by the methods used. For example, erythropoiesis might have been inhibited had the plasma been given for a longer time.

Discussion

The association between thymic tumours and red-cell aplasia is sufficiently well established to suggest a causal relationship, but this has never been demonstrated experimentally. Loeb (1956) failed to reproduce anaemia when he injected 250 ml. of fresh plasma from a patient with a benign thymoma and red-cell aplasia into a normal adult recipient. Our patient's plasma produced no demonstrable effect on erythropoiesis when injected into normal rats in proportionately much greater amounts. These studies thus fail to provide experimental evidence of a humoral mechanism.

In our patient thymectomy had no demonstrable beneficial effect, whereas subsequent prednisone therapy was associated with a complete haematological remission which was maintained until the patient's death from other causes two months later.

Six of the 10 patients in whom the results of thymectomy have been reported (Soutter *et al.*, 1957) have had a haematological remission at some stage after operation, but in only two (Humphreys and Southworth, 1945; Barquet Chediak *et al.*, 1953) was this immediate, maintained, and unassociated with other therapy or operation. Chalmers and Boheimer (1954) reported the successful use of corticotrophin after thymectomy and splenectomy in two patients. Neither of the patients of Ross *et al.* (1954), however, improved despite

the use of corticotrophin after thymectomy in one and splenectomy and thymectomy in the other. The pathogenesis of this condition remains obscure, but these various results of treatment are compatible with the concept that thymectomy may result in the removal of an inhibiting humoral factor, so allowing normal erythropoiesis to take place either spontaneously or under the influence of steroids.

Summary

A case of benign thymoma and red-cell aplasia is described. Thymectomy did not produce a haematological remission, but normal erythropoiesis occurred later during treatment with prednisone. The patient's plasma did not inhibit erythropoiesis when injected into normal rats.

We are indebted to Dr. W. Phillips, under whose care this patient was admitted; to Dr. J. D. P. Graham for assistance with the animal experiments; to Mr. R. G. Wood for help with the isotope studies; and to Mr. D. M. E. Thomas and Dr. R. M. E. Seal, of Sully Hospital. Facilities for doing the experimental studies were made available to one of us (G. S. K.) during the tenure of a Research Fellowship in Medicine in the Royal Infirmary, Cardiff.

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ROLE OF OSMOTIC DIURESIS IN IMPAIRMENT OF CONCENTRATING ABILITY IN RENAL DISEASE

BY

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It has been suggested by Platt (1952) that the loss of "concentrating power" (osmotic ceiling), which is so constant a feature of chronic renal insufficiency, might be, at least partly, due to osmotic diuresis. He pointed out that in nephropathies there often is anatomical as well as functional evidence of increased activity per nephron. Osmotic diuresis may be constantly present in these conditions, not only as a result of elevated blood levels of solutes—for example, of urea—but also by an increased filtration rate per nephron.

Direct proof of this attractive hypothesis has not yet been given. Several authors (Nickel *et al.*, 1953; White and Rubin, 1954; Bull, 1956) have reported a linear relationship between flow and load in their patients, which they regarded as an argument for the presence of osmotic diuresis. This, however, is not conclusive, because such relationships may also be observed under normal conditions—for example, during a concentration test (McCance, 1945) or during maximal water diuresis (Schoen, 1957).

To determine whether and to what extent osmotic diuresis is responsible for the loss of concentrating power in a particular patient, his flow–load relations must be compared with those of normal people.

In normal man, during acute experiments and maximal antidiuretic hormone activity, osmotic diuresis is characterized by a certain relation between urine flow and concentration (Rapoport *et al.*, 1949). In most cases this relation can be expressed by the formula:

$$\frac{C_u}{C_p} = \frac{V+A}{V} \quad \text{.....Formula 1}$$

where C_u and C_p represent total osmolar concentration in urine and plasma, V the urine flow, and A a quantity of water which if added to the urine would make it iso-osmolar with the plasma. This factor A has been called "water economy" (West and Rapoport, 1950) or "negative free water clearance," and reaches a maximum which is designated as T^cH_2O by Smith and his school. When, at a certain flow, this maximum has been reached it can thus be calculated:

$$T^cH_2O = V\left(\frac{C_u}{C_p} - 1\right) \quad \text{.....Formula 2}$$

In order to investigate the question to what extent osmotic diuresis is present under conditions of everyday life in renal patients, we have established the "flow–load relation" in these patients during maximal antidiuresis with and without additional osmotic loading and compared the results with those obtained in normal people under the same conditions.

Materials and Methods

All patients were submitted to a standard concentration test and to a mannitol infusion. These experiments were often done in succession. When we were afraid that severe fluid deprivation would not be well tolerated, thirsting was reduced to 12 hours and a pitressin-tannate-in-oil injection was given in addition, to provide for maximal antidiuresis. Mannitol was infused as a 15% solution in amounts varying from 75 to 150 g., during one to one and half hours. After the infusion was finished, urine was collected in portions of 100–200 ml. by spontaneous voiding, in at least four successive periods. Osmolarity was measured by freezing-point determination according to the Johlin (1931) principle. For calculation of the T^cH_2O we used the average "water economy" (formula 2) from all periods during which serum mannitol concentrations were at least 350 mg. per 100 ml.

The subjects were divided into four groups. Group 1 consisted of 10 normal persons. One of these subjects (No. 1 in the Table) was examined several times in different circumstances. The flow–load relation curve thus obtained was used as a standard with which the results obtained with the other individuals were compared.

In group 2 the data were collected from nine patients with probably chronic nephritis, and in group 3 from five patients in whom predominant tubular damage could be expected—two with hypercalcaemia whose history is reported elsewhere (Dorhout Mees, 1957); two with tubular necrosis 32 and 28 days respectively after the beginning of anuria; and one with unexplained renal diabetes insipidus. Group 4 is a miscellaneous group, including two patients with one kidney, one with renal vein thrombosis, and two others in whom renal impairment of undetermined origin was found accidentally.

Results

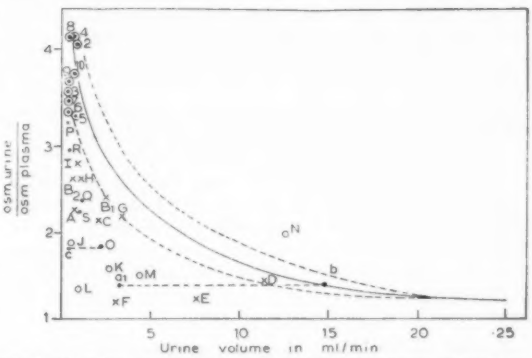
The Table gives a survey of the data obtained. The T^cH_2O value was calculated as the mean of at least four measurements. For the "standard person" (No. 1) this value was calculated as the mean of 34 determinations, obtained during four experiments. These experiments were done under conditions of different salt intake, while the load was once in urea and three times in mannitol. The T^cH_2O values showed considerable variations (from 3.9 to 6.6) in the various experiments. The mean value of 5.7 was arbitrarily chosen as a standard reference to which the T^cH_2O values of the others, normals as well as patients, were related.

In column 4 this relation is given as a factor (k) by which the T^cH_2O value should be multiplied to make it equal to 5.7.

The last three columns (5, 6, and 7) give the urine/plasma (U/P) osmolar maximum during thirsting, the urine volume at which this was reached, and the time of dehydration used. For graphical representation of the flow–load relation it seemed more appropriate to relate the urine osmolar concentration $\left(\frac{\text{load}}{\text{flow}}\right)$ with urine flow instead of the load itself, and to express total urine osmolar concentration by the osmolar urine/plasma ratio.

In the Chart the mean of all observations and the control limits of the "standard person" are given as the drawn line and the dotted lines respectively, showing a flow–load relation which is similar in shape to that obtained by Rapoport *et al.* (1949), though not quite identical with it.

In order to compare flow–load relations observed in the other persons with this particular flow–load relation,



Maximal urine concentration at low urine flows related to corresponding flows, after "correction" of the latter by factor k. For further explanation see text.

we have multiplied the diuresis values of each person by the above-mentioned factor k, which results in a displacement of the point in a horizontal level in the Chart. For the sake of simplicity in the Chart only one point of each patient is shown. For this point we chose the observation during which the highest urine concentration was measured—that is, the left-hand end of each curve.

As an example we demonstrate the procedure on patient O, whose T^cH_2O was nearly constant (1.1 ± 0.06) during six observations. During the first period a U/P osmotic concentration ratio of 1.34 was found, the urine production being 3.2 ml./min. This is represented by point a in the Chart. After multiplication of the urine flow value with factor k (5.2 in this case) the point is displaced to the right. It is clear that it will coincide with the drawn line (point b), as factor k was given just that value that would make flows in the range where T^cH_2O is reached (i.e. water reabsorption is maximal) identical with those produced by the standard person at the same urine concentration. When the urine flow (0.40 ml./min.) observed during the highest U/P ratio (1.8) is multiplied by factor k, point c (representing this low urine flow) is also displaced to the right, which results in point O—that is, not on the "standard curve."

It is obvious that in the hypothetical case the renal tissue of the standard person could be reduced in amount but remain qualitatively normal in all respects, all the points from the regression curve would be displaced to the left, the different urine flows being reduced in a constant proportion. Multiplication of the flows with the reverse of this factor would again reproduce the original line. In the case of patient O and of the other patients, there cannot be found any one factor that would make the flow–load relations identical with those of the standard person in the entire flow range.

Data Obtained from the Four Groups

Subject	Diagnosis	Sex	T^cH_2O	Factor k	U/P Osmolar Maximum	Urine Volume During Max. Conc.	Hours of Dehydration (Conc. Test)
			Group 1				
1	Normal	M	5·7	1	4·1		
2	"	M	6·1	0·93	4·0	0·50	18
3	"	M	5·1	1·12	3·6	0·20	20
4	"	M	5·3	1·07	4·1	0·42	16
5a	"	F	4·9	1·16	3·6	0·5	20
5b	"	F	4·7	1·21	3·6	0·5	20
6	"	M	5·7	1	3·4	0·32	22
7	"	M	5·2	1·10	3·5	0·28	20
8	"	M	6·0	0·95	4·1	0·39	19
9	"	M	6·0	0·95	3·7	0·35	24
10	"	M	5·4	1·06	3·8	0·45	24
			Group 2				
A	Chronic nephritis	M	2·5	2·3	2·2	0·38	24+P
B 1	"	F	1·6	3·6	2·4	0·62	24
B 2	"	F	1·4	4·1	2·5	0·16	26
C	"	M	1·5	3·8	2·1	0·5	30
D	"	F	0·16	35	1·4	0·5	30
E	"	M	0·5	11·4	1·2	0·7	14+P
F	"	M	0·4	14	1·3	0·22	19+P
G	"	M	1·1	5·2	2·2	0·55	19+P
H	Acute nephr., recovering	M	3·2	1·8	2·5	0·44	26
I	Chronic nephritis, dubious	M	2·9	2·0	2·6	0·45	24
			Group 3				
J 1	Hyperparathyroidism	F	1·7	3·4	1·9	0·32	26
J 2	"	F	1·1	5·2			
K	Vit. D intox.	F	1·1	5·2	1·55	0·54	25
L	Tubular necr.	F	1·9	3·0	1·45	0·36	20+P
M	" "	M	1·5	3·8	1·5	1·55	17+P
N	Renal diab. insip.	M	0·65	9	1·8	1·4	24+P
			Group 4				
O	Renal vein thrombosis	F	1·1	5·2	1·8	0·40	20+P
P	Hypoplasia of one kidney. Hypertension	M	3·1	1·8	3·3	0·25	20+P
Q	Nephrectomy	M	4·4	1·3	2·3	0·7	20+P
R	Unknown (nephrolithiasis ?)	M	4·0	1·4	2·8	0·3	24
S	(Hypertension)	M	2·7	2·1	2·2	0·35	36

Discussion: Theoretical Considerations

The renal capacity for active water reabsorption seems to be limited by two factors—the osmotic ceiling at low flows and a volume transportation capacity (T^cH_2O) at high flows.

So far it is assumed that T^cH_2O indicates a renal tubular function and that one can speak in terms of T^cH_2O for each nephron. The findings that T^cH_2O is influenced by the state of hydration (Epstein *et al.*, 1957a) and the protein intake (Epstein *et al.*, 1957b) are not in contradiction with this assumption. More difficult to explain are the divergent values found during sodium (Ladd, 1951) or mercurial (Grossman *et al.*, 1955) diuresis and after loading with mannitol (Zak *et al.*, 1954). Curiously enough, this fact has not attracted much attention.

The occasional reports of hypotonic urines in osmotic diuresis during hydropenia (Mudge *et al.*, 1949; Zak *et al.*, 1954; Anslow and Wesson, 1955), and the observations of De Wardener and del Greco (1955) suggesting hypotonicity in the proximal tubules, throw further doubt on the "classic" theory. If the attractive views of Wirz (1957) are true, revision of many theoretical constructions will be necessary. Even then, however, it is to be explained why in many instances the value of the T^cH_2O remains so constant.

As Bull (1956) stated, it is not possible to compare experiments in different individuals, as the number of nephrons is unknown and there may be various degrees of glomerular and tubular hypertrophy, which complicate experimental approaches.

This matter may nevertheless be simplified by stating that flow–load relation is a question of balance between excreted load and faculties of renal water reabsorption. If osmotic diuresis is substantially depressing urine concentration, it is more specifically a question of balance between excreted load and T^cH_2O. It is obvious that comparison of results obtained in different persons is hampered by the differences in this T^cH_2O value.

In order to obtain the same relation between load and T^cH_2O for all persons, the "correction factor" k was introduced, making the T^cH_2O (whatever may be its physiological significance) equal to that of the standard person.

In this way, flow–load relations at high flows are arbitrarily made to coincide, and if the only difference between the subjects would have been a different amount of (qualitatively normal) renal tissue, flow–load relations at lower flows would also fall into the same range.

It is clear that values of the other normal people show close agreement with the standard regression line, whereas those of the patients (with one exception) fall to the left and below this line.

If osmotic diuresis were the only factor limiting urine concentration, there is no reason why the concentrations at the "corrected" urine flows would not reach normal values. It appears, however, that most of our patients were not able to reach as high a concentration gradient between urine and plasma as were the normal people, at a same relation between excreted load and maximal water reabsorption capacity.

This fact, indicating that the osmotic ceiling was relatively more depressed than could be accounted for by osmotic diuresis, may, however, not be a proof of tubular cell damage. It may be that normal functioning of the concentrating mechanism is possible only in the presence of a normal renal architecture and is readily disturbed by scarring, occlusion of blood vessels, and the presence of non-functioning tubuli, as can be expected from Wirz's conceptions. It was expected that patients with one normal kidney would have a normal osmotic ceiling, if correction was made for osmotic diuresis. This was indeed the case in patient Q, but not in patient R. Perhaps there are still other reasons for loss of concentrating power. We sometimes observed that, at the end of osmotic diuresis experiments, a more concentrated urine was produced (at higher loads) than during dehydration with minimal load.

Summary and Conclusions

Measurements were made of maximum urine osmolar concentration, T^cH_2O, during mannitol loading and mannitol clearance in normal people and in patients with several forms of renal disease. The results are discussed in the light of the hypothesis that constant osmotic diuresis may be responsible for diminished urine concentration in renal disease.

It is concluded that the loss of "concentrating power" cannot be accounted for entirely by the effect of osmotic diuresis in patients with chronic glomerulonephritis or other disturbances. Specific damage to tubular function seems to be of more importance.

The significance of the T^cH_2O concept is critically discussed. It is suggested that disturbance of tubular water reabsorption reflects not only tubule cell damage but also disturbance of renal architecture.

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Turkeys, ducks, and pigeons have now joined parrots on the danger list of public health as transmitters to man of a generalized virus infection known as psittacosis or ornithosis. Ninety-eight species of birds (57 of them belonging to the parrot and parakeet family) have been found to be naturally infected with this disease, which is by no means always benign in man, since until recently it killed 2.6% of its victims. With modern antibiotic treatment the number of deaths has been considerably lowered. . . . Epidemics have been reported from many countries, including the U.S.A., Canada, Czechoslovakia, Austria, the U.S.S.R., Germany, etc. So far as is known, the disease has never been contracted from eating diseased birds. Addition of tetracycline compounds to poultry feed has been successful in eradicating the infection from a few parakeet-breeding aviaries, but the results with pigeons and turkeys have been less promising; it is hoped, nevertheless, that a suitable chemotherapeutic method can eventually be developed (Dr. K. F. Meyer, *W.H.O. Bulletin*, Vol. 20, No. 1, 1959).

RELATION BETWEEN MAXIMAL URINE CONCENTRATION, MAXIMAL WATER REABSORPTION CAPACITY, AND MANNITOL CLEARANCE IN PATIENTS WITH RENAL DISEASE

BY

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Despite the increase in our knowledge concerning renal physiology, there seems to be little need for more elaborate techniques in the evaluation of renal patients. Routine urine analysis, the "concentration test," and urea or creatinine clearance indeed give nearly maximal information about diagnosis and prognosis in most cases.

Recently the value of the "classical" concentration test has again been challenged. Not only has the determination of the freezing-point depression (which was abandoned some 50 years ago) been advocated instead of the specific gravity (Frank *et al.*, 1957), but the whole question of the value of measuring concentration ability at low flows has been a matter of dispute. Baldwin *et al.* (1955) stated that (concerning water conservation) "the basic physiological operation of the kidney can only be judged in terms of the quantity of water abstracted."

It is the purpose of this communication to determine whether measuring of the maximum water reabsorption (T^cH_2O) would give more useful information than the concentration power, measured as the maximum osmolar urine/plasma (U/P) ratio. We do not intend to comment on the correlation between osmolar concentration and specific gravity, which has been extensively investigated (Miles *et al.*, 1954; Dorhout Mees, 1957).

Materials and Methods

The normal persons and the patients investigated were the same as in the previous communication (Dorhout Mees, 1959); the methods of determining maximum U/P ratio and T^cH_2O are described there. The mannitol clearance was determined in the same urine samples as was the T^cH_2O (usually the mean of four successive periods). The normal clearance values obtained in this way were lower than those found by most investigators, as was reported elsewhere (Dorhout Mees *et al.*, 1958). However, we assume that it reflects glomerular function with sufficient accuracy.

Results

Data Obtained from the Four Groups

Subject	Diagnosis	Sex	C Man	T^cH_2O	$\frac{T^cH_2O}{C\ man} \times 85$	U/P Osmolar Maximum
			Group 1			
1	Normal	M	86	5·7	5·7	4·1
2	,,	M	86	6·1	5·0	4·0
3	,,	M	90	5·1	4·8	3·6
4	,,	M	76	5·3	5·9	4·1
5a	,,	F	75	4·9	5·5	3·6
5b	,,	F	79	4·7	5·0	
6	,,	M	81	5·7	6·0	3·4
7	,,	M	89	5·2	5·0	3·5
8	,,	M	87	6·0	6·1	4·1
9	,,	M	78	6·0	6·5	3·7
10	,,	M	95	5·4	4·8	3·8
			Group 2			
A	Chron. nephritis	M	53	2·5	3·6	2·2
B1	,, ,,	F	40	1·6	3·3	2·4
B2	,, ,,	F	41	1·4	2·9	2·5
C	,, ,,	M	34	1·5	3·7	2·1
D	,, ,,	F	24	0·16	0·7	1·4
E	,, ,,	M	24	0·5	1·7	1·2
F	,, ,,	M	12	0·4	2·9	1·3
G	,, ,,	M	36	1·1	2·6	2·2
H	Acute nephr., recovering	M	57	3·2	4·9	2·5
I	Chron. nephr., dubious	M	71	2·9	3·7	2·6
			Group 3			
J1	Hyperparathyroidism	F	51	1·7	2·0	1·9
J2	Hyperparathyroidism	F	58	1·1	1·6	
K	Vit. D intox.	F	29	1·1	3·15	1·55
L	Tubular necr.	F	62	1·9	2·6	1·45
M	,, ,,	M	50	1·5	2·5	1·5
N	Renal diab. insip.	M	56	0·65		1·8
			Group 4			
O	Renal vein thrombosis	F	21	1·1	4·8	1·8
P	Hypoplasia of one kidney. Hypertension	M	56	3·1	4·5	3·3
Q	Nephrectomy	M	68	4·4	5·1	2·3
R	Unknown (nephrolithiasis ?)	M	64	4·0	5·3	2·8
S	(Hypertension)	M	68	2·7	3·4	2·2

The Table summarizes the patients and the data obtained. In the sixth column the ratio of T^cH_2O to mannitol clearance is given, multiplied by our normal mean of the latter. The letters and numerals in Figs. 1–3 relate to patients listed in the Table.

In Fig. 1 we have correlated U/P maximum (during "conventional" concentration test) and T^cH_2O values. There is a rough linear correlation.

In Fig. 2 $\frac{T^cH_2O}{C\ man} \times 85$ is related to the mannitol clearance (C man). The shaded area includes those cases in which this value is in the normal range, although both T^cH_2O and mannitol clearance may be substantially reduced.

Finally, Fig. 3 gives the correlation of mannitol clearance and maximum U/P ratio.

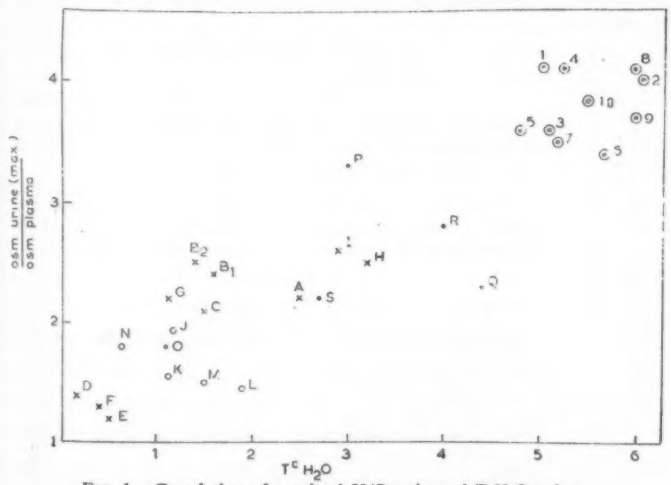

FIG. 1.—Correlation of maximal U/P ratio and T^cH_2O values.

Discussion

It is to be expected that maximal U/P concentration ratio and T^cH_2O are in some way related to each other,

and that a tubule with a lowered reabsorption capacity cannot attain a normal concentration. In the first publication on the T^cH_2O determination in renal disease Baldwin *et al.* (1955) stressed the poor correlation between concentration ability as measured by specific gravity and T^cH_2O. We did not observe such extreme divergencies between urinary specific gravity and osmolarity during concentration tests. We did not find much variation in the relation between T^cH_2O and maximal urine osmolarity, as is shown in Fig. 1.

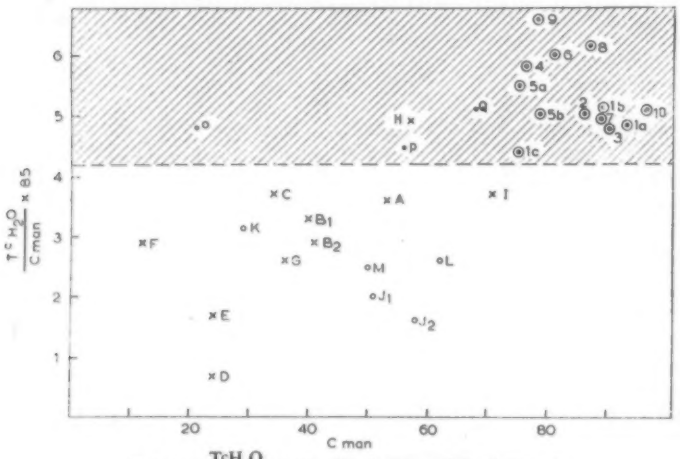

FIG. 2.—$\frac{T^cH_2O}{C\ man.} \times 85$ related to mannitol clearance.

However, we found Baldwin's data, when arranged in the same way, to be in about the same range, with two exceptions in which a normal T^cH_2O was associated with a very low U/P maximum.

The fact that, as shown in Fig. 1, both limits of the concentration power are usually depressed roughly to the same extent for all three groups of patients can be explained on the basis both of tubular damage and of a relative overburdening of the nephrons with resulting osmotic diuresis. Consequently the nature of the renal condition does not appear to influence this relationship. Dunstan *et al.* (1956) suggest that, after correction of potassium loss, the previously depressed T^cH_2O and maximum U/P ratio are not restored to the same extent, but in these cases the maximum U/P ratio remained the most abnormal one.

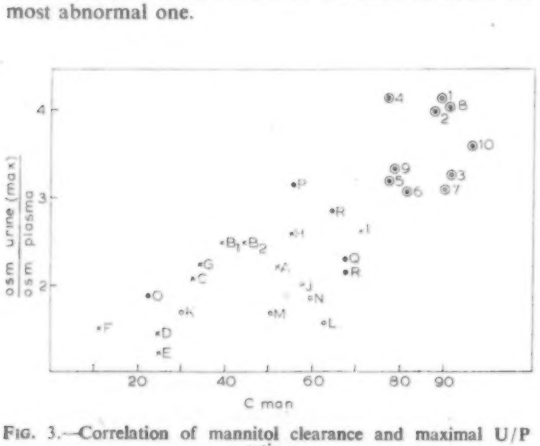

FIG. 3.—Correlation of mannitol clearance and maximal U/P ratio.

If our own results as well as those of others are taken into account, it seems to us that determination of the maximum U/P ratio is still the most sensitive means of testing the integrity of the renal water-conservation system. We found no indication that determination of T^cH_2O yields valuable aids in differential diagnosis. The consideration that the latter "more accurately reflects the basic physiological process"—that is, of water reabsorption—is rather theoretical, there being no indication that measurement of the maximal capacity of this process during rather unphysiological circumstances (osmotic diuresis) gives more accurate information about any actual renal function in disease.

All our patients showed abnormal values for T^cH_2O and mannitol clearance values. The results are in accordance with those of Baldwin *et al.* for the majority of patients with chronic nephritis.

It is apparent that if active water reabsorption would be depressed to the same extent as glomerular filtration the quotient $\frac{T^cH_2O}{C\ man} \times 85$ should be independent of the filtration rate (mannitol clearance). From Fig. 2 it is clear that, regardless of the nature of the renal disease, there is a tendency for the T^cH_2O to be relatively more depressed than the mannitol clearance as renal failure is more pronounced. In patients with specific tubular damage (group 3) the T^cH_2O depression is of course very striking, especially at higher clearance rates. For differential diagnostic purposes, however, the relative depression of U/P osmolar maximum is by no means less striking, as is shown in Fig. 3. This, too, illustrates in a different way the fact that determination of T^cH_2O is not superior to U/P maximum determination for evaluating the water-conservation power of the renal tubules.

Summary

In order to evaluate the importance of T^cH_2O determination for clinical purposes, the results of this determination after mannitol infusion were compared with maximum osmolar U/P ratio and mannitol clearance in a number of normal persons and in patients with a variety of renal diseases.

It is concluded that T^cH_2O determination is not superior to maximum osmolar U/P ratio obtained during a conventional concentration test for detection of tubular or overall kidney damage.

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A CONGENITAL BLOOD-CLOTTING ANOMALY RESEMBLING COUMARIN-INDUCED DEFECT

BY

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In spite of the various investigations carried out on the blood-clotting defect caused by the administration of coumarin drugs, their precise mode of action is still undetermined. It is, however, generally agreed that they produce a diminution in the concentration of prothrombin in plasma (Roderick, 1931 ; Quick, 1937), delay the conversion of prothrombin to thrombin by brain extract (Owen and Bollman, 1948), and reduce the formation of plasma thromboplastin (Biggs, Douglas, and Macfarlane, 1953). Recent studies revealed that the latter defect is most probably due to a deficiency of Christmas factor (Sise, Kimball, and Adamis, 1955 ; Douglas, 1955 ; Naeye, 1956 ; Douglas and Mair, 1958), and Prower factor (Denson, 1958).

The purpose of this paper is to present a case with a congenital blood-clotting defect simulating that produced by coumarin drugs.

Case Report

The patient was first seen at the age of 6 years, one week after eight teeth had been extracted. Bleeding from the sockets had continued for six days despite plugging. One month prior to this he had a mild attack of epistaxis. At the age of 5 years a small cut of the skin over the right eye did not cause much trouble. No history of haematuria, melaena, haematemesis, haemarthrosis, or spontaneous bruising could be elicited. He was of normal appearance and intelligence. No abnormality was detected on physical examination. Examination of the nasal passages showed no vascular abnormalities. Both the capillary fragility (Hess test) and the bleeding-time were normal. Laboratory tests carried out at that time showed that the one-stage prothrombin time was prolonged. Accordingly he was given a course of vitamin K, 30 mg. daily for nearly eight months. Unfortunately, he was not seen for the next five years. During this period he continued to suffer from mild attacks of epistaxis mostly from the right side and occurring more often in the summer. Skin cuts, however, seemed to heal satisfactorily.

On the patient's recent attendance for the extraction of five teeth a more detailed study of the clotting defect was carried out ; the results are presented below. Removal of the teeth was followed by a slight oozing of blood for 48 hours, but no transfusion was required.

The patient's paternal aunt and grandfather had a history of bleeding after teeth extractions. These subjects, however, were not available for investigation.

Investigations

The blood-clotting tests were carried out essentially as described by Biggs and Macfarlane (1957). The results (Table I) show that the blood and plasma clotting-times and the prothrombin consumption index are within normal range, while the one-stage prothrombin time is prolonged. The latter is corrected by the addition of 10% normal serum or normal plasma, but not by $Al(OH)_3$-treated plasma or plasma from a patient receiving coumarin drugs. Since the latter two reagents contain factor V, but little prothrombin and factor VII, its lack of effect on the one-stage prothrombin time demonstrates the absence of factor V deficiency. On the other hand, serum contains factor VII and normal untreated plasma contains both factor VII and prothrombin. The shortening of the prothrombin time by these two reagents indicates that the patient's plasma is deficient in factor VII and possibly prothrombin.

The estimation of prothrombin by the two-stage method demonstrated that both factors were deficient. The results obtained using this test are illustrated in the Chart. Analysis of the two curves in this figure shows that the peak of the concentration of thrombin formed in the patient's plasma is delayed. This delay can be encountered in either factor V or factor VII deficiency. Since the former anomaly has already been excluded by studying the effect of different reagents (Table I) on the one-stage prothrombin time, this would appear to incriminate factor VII. The Chart also shows that the area covered by the patient's curve is equal to 68% of that covered by the normal, indicating a prothrombin concentration of this magnitude in the patient's plasma.

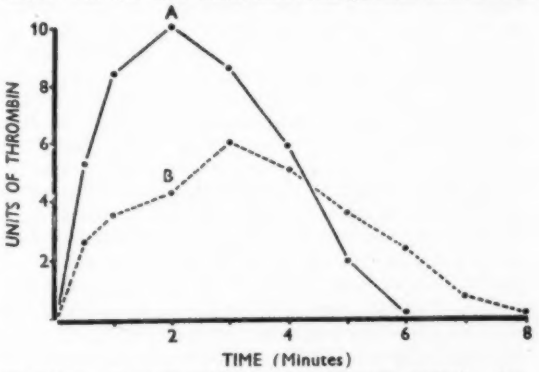
TABLE I.—*Blood-clotting Tests*

Test	Normal	Patient
Whole-blood clotting-time (min.) ..	4–7	5½
Plasma clotting-time (min.)	2–4	3½
Prothrombin consumption index (%) ..	<40, usually <10	6
One-stage prothrombin time (sec.) ..	11–12	20
,, ,, ,, adding 10% Normal $Al(OH)_3$-treated plasma ..	—	20
,, serum	—	15
,, plasma	—	16
Factor-VII-deficient serum*	—	19½
Plasma with coumarin-induced defect†	—	20½

* Obtained from a patient with this congenital defect, one-stage prothrombin time being 17 seconds.
† Patient receiving phenindione; one-stage prothrombin time 27 seconds.

The thromboplastin generation test demonstrated that the $Al(OH)_3$-treated plasma of the patient did not lack either antihaemophilic globulin or factor V and did not contain an anticoagulant. On the other hand, it indicated that his serum was deficient in a factor necessary for the formation of plasma thromboplastin. This defect was corrected by normal or Christmas disease serum (Table II), but was unaffected by serum obtained from patients receiving ethyl biscoumacetate or phenindione.

Effect of Factor-VII-deficient Serum.—Although it is now believed that factor VII is not essential in the formation of plasma thromboplastin (Ackroyd, 1956), it was thought advisable to study the effect of serum procured from a patient with this congenital anomaly. This did not influence the one-stage prothrombin time (Table I), but it shortened the substrate clotting-time in the thromboplastin generation test from 25 to 16½ seconds, thus denoting and confirming that factor VII is not the only factor lacking in the patient's blood. On the other hand, sera from patients treated with



Estimation of prothrombin by the two-stage method. A= Normal plasma. B=Patient's plasma.

TABLE II.—*Effect on Thromboplastin Generation Test of Adding Various Sera to the Patient's Serum*

Serum Incubated with $Al(OH)_3$-plasma, Platelets, and 0·025 M $CaCl_2$	Substrate Clotting-Time‡ (sec.)
Normal serum	10
Patient's ,,	25
Serum of patient receiving ethyl biscoumacetate	43
,, ,, ,, ,, phenindione	29½
Christmas disease serum	38
Patient's serum mixed with 10% of:	
Normal serum	16
Serum of patient receiving ethyl biscoumacetate*	27
,, ,, ,, ,, phenindione†	25
Christmas disease serum	18
Congenital factor-VII-deficient serum§	16½

* One-stage prothrombin time 42 seconds (normal 12 seconds).
† One-stage prothrombin time 29 seconds (normal 11 seconds).
‡ The activity of thromboplastin produced in each mixture was tested after six minutes by taking 0·1 ml. thereof together with 0·1 ml. of 0·025 M $CaCl_2$ and adding them simultaneously to 0·1 ml. of normal citrated plasma (substrate) at 37° C., recording the clotting-time.
§ This gave normal results (10 seconds) when tested by the thromboplastin generation method.

ethyl biscoumacetate or phenindione were ineffective in correcting the clotting defect (Tables I and II). Similarly, the coumarin-induced defect was not corrected by the patient's plasma or serum.

Liver-function Tests.—Paper electrophoresis of serum, using barbitone buffer *p*H 8.6, showed normal bands. Serum thymol turbidity was 0.2 unit and serum alkaline phosphatase 22 units.

Effects of Vitamin K.—The blood-clotting tests were repeated before and during a course of vitamin K, 40 mg. daily for four weeks. The blood-clotting defect was not affected by this treatment. Furthermore, the clinical picture was not improved, the patient having an episode of epistaxis while receiving the drug.

Examination of Father's Blood.—This was found to be normal.

Discussion

The condition described in this paper seems to be a congenital anomaly; the haemorrhagic tendency appeared before the age of 6 in the patient, who received no coumarin drugs. The results of the blood-clotting tests are similar to those found in patients receiving these drugs. Thus the patient has normal blood and plasma clotting-times but a prolonged one-stage prothrombin time, and his serum is lacking in factor(s) necessary for the generation of normal levels of plasma thromboplastin (Biggs *et al.*, 1953). Furthermore, the two-stage method shows that the concentration of prothrombin is below normal levels and demonstrates a retardation in the conversion of this factor to thrombin. Unlike the coumarin defect, however, the patient's deficiency was not influenced by vitamin K therapy.

Walker and Hunter (1954) provided evidence which suggested that the action of coumarin drugs on the blood-clotting mechanism is not restricted to prothrombin and factor VII only; another factor, termed factor X, was, in addition, thought to be involved. This view has been followed by various reports which seem to indicate that these drugs produce multiple defects (Koller, 1955; Biggs, 1956; Greig and Tattersall, 1956), the exact nature of which is still far from being solved. Whatever the final outcome of further investigations in this respect, however, it is apparent that the blood-clotting factors affected by these drugs are also lacking in the blood of our patient, as can be deduced from the failure of mutual correction.

Several workers have described cases in which plasma gave an abnormal one-stage prothrombin time. Some of these were presumed to be due to a deficiency of factor VII and have been reviewed by Ackroyd (1956). Patients diagnosed as having hypoprothrombinaemia have been mentioned by Biggs and Macfarlane (1957). Of the recorded cases, only those described by Newcomb *et al.* (1956) and Biggs (1956) seem to bear some resemblance to our patient.

Summary

The clinical features of a patient with a mild haemorrhagic diathesis are reported. Laboratory investigations demonstrated that, although the congenital blood-clotting defect is basically similar to that produced by coumarin drugs, no improvement was achieved by vitamin K therapy.

We thank the Department of Medical Illustration, Manchester Royal Infirmary, for help in preparing the Chart.

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EFFECT OF CASTOR OIL, SOAP ENEMA, AND HOT BATH ON THE PREGNANT HUMAN UTERUS NEAR TERM

A TOCOGRAPHIC STUDY

BY

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The administration of castor oil, followed by a soap enema and a hot bath, is probably one of the oldest and most frequently attempted methods of inducing labour. This regime is also used as a complement to other induction procedures, such as an oxytocin ("pitocin") drip or surgical rupture of the membranes.

Recently, however, some obstetricians have tended to regard castor oil as an ineffective oxytocic drug and have abandoned its use altogether in the induction of labour. Nabors (1958) carried out a clinical trial of the effectiveness of "rupture of membranes and pitocin" either alone or combined with castor oil or enema, or castor oil and enema together. On the basis of his findings he concluded that castor oil is of no value in the induction of labour. However, a study of his figures shows that there were fewer "failed inductions" in the group which was given castor oil.

Castor oil has so many unpleasant features, such as its taste and its tendency to produce nausea, vomiting,

and diarrhoea, that its continued use is justified only if it is a reasonably effective oxytocic.

It was for this reason that we decided to assess, with the aid of a tocograph, the possible effects of castor oil, a soap enema, and a hot bath upon uterine contractility in late pregnancy.

Material and Methods

Sixty subjects, all between 38 and 41 weeks pregnant, were selected for the investigation and divided into four groups of 15. Cases of cephalo-pelvic disproportion, malpresentation, ante-partum haemorrhage, hydramnios, and those showing any sign of the onset of labour were excluded.

Castor oil, a soap enema, and a hot bath (a "complete O.B.E.") were administered to each subject in the first group; only castor oil was given to those in the second, only a soap enema to those in the third, and only a hot bath to those in the fourth group. The changes in uterine activity in each case were assessed by the use of the guard-ring tocodynamometer described by Smyth (1957). Smyth claims that this instrument can provide an absolute measurement of the changes in intra-amniotic pressure, and thus of the uterine contractions.

In conformity with Smyth's recommendations the head of the instrument was applied to the anterior abdominal wall over a fluid-filled part of the uterus and held in place by a stiff elastic belt passed around the subject.

With the head of the instrument in the same position on the abdominal wall and the elastic belt at the same tension, a recording was taken in each case before and after the four different methods adopted. Each tracing was recorded for at least one hour on a chart moving at a constant speed of 12 in. (30.5 cm.) an hour.

In order to assess accurately the extent of change in the uterine contractions the instrument was also calibrated according to the directions of Smyth (1957).

Method of Assessing Effect of Complete O.B.E.—In this group the first recordings were taken within 12 hours before the administration of the O.B.E. Castor oil, 2½ oz. (71 ml.), was given by mouth, and after two bowel actions, usually within three hours, this was followed by a soap enema (2 oz. (57 ml.) of enema soap in 2 pints (1,140 ml.) of water at blood heat). The enema was allowed to act and the subjects were then given a hot bath. This completed, they were returned to bed and the second tracing was started.

Method of Assessing Effect of Castor Oil.—Castor oil, 2½ oz. (71 ml.), was administered by mouth to the 15 subjects in this group at the completion of the first recording. The second recording was started after at least two bowel actions, again usually within three hours of the administration of the castor oil.

Method of Assessing Effect of Soap Enema.—In this group a soap enema was administered at the completion of the first recording and the second tracing started after the enema had acted.

Method of Assessing Effect of Hot Bath.—The tracings were taken in this group just before and immediately after the subjects had been given a hot bath.

Interpretation of Tracings

From a careful study of the two tracings from each subject, the work done by the uterus in contracting before and after the administration was compared.

From the two tracings obtained in each subject the amplitude in grammes per square centimetre and the duration of each contraction in minutes and their frequency were calculated.

According to Reynolds *et al.* (1954) the sum of the areas of all contractions in a given time unit is an index of the contractile work of the uterus in that time. With his indirect method the product of the duration and the amplitude of each contraction and the number of contractions per hour yielded an index of the total contractile work done by the uterus in that hour.

To exclude the minor variations in uterine tone (Alverez and Caldeyro Barcia, 1953) amplitudes of less than 10 g. per sq. cm. were excluded from the assessment.

In each case the index of contractile work done by the uterus per hour before and after the treatment was determined and the percentage difference calculated.

Control Group.—Study of tracings of uterine contractions recorded for one hour often shows some minor spontaneous variation in activity during this time. This constitutes a possible source of error when comparing tracings from the same individual taken several hours apart. In order to assess the accuracy of the results a control group of 15 other subjects, comparable in every way to those in the other four groups, were chosen. In each of these the two tracings were taken three hours apart, with the head of the

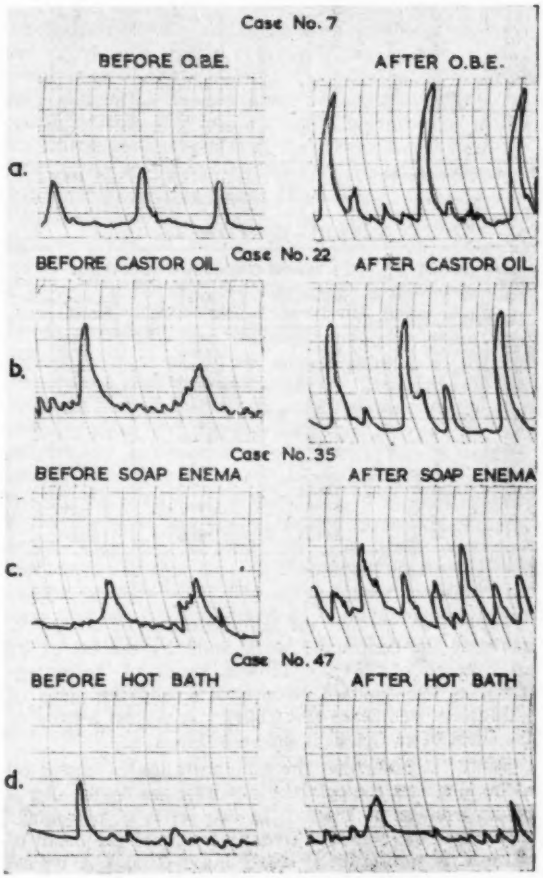

FIG. 1.—Sections of typical tracings.

instrument in the same position and the elastic belt at the same tension but with no treatment in the interval.

Results

The results are shown in Tables I–V.

TABLE I.—*Effect of Complete O.B.E.*

Case No.	Gravidity	Index of Contractile Work of Uterus		
		Before O.B.E.	After O.B.E.	Increase after O.B.E.
1	M	195·75	897·75	+359%
2	M	260·0	1,199·5	+361%
3	P	312·5	1,139·25	+265%
4	P	552·75	1,062·75	+92%
5	M	83·75	253·5	+203%
6	P	109·75	581·0	+429%
7	P	218·0	705·75	+224%
8	M	360·0	1,082·75	+201%
9	M	202·25	269·0	+33%
10	P	92·5	223·5	+142%
11	M	241·75	308·5	+28%
12	P	76·25	711·0	+833%
13	P	234·25	1,021·75	+336%
14	P	87·75	203·5	+132%
15	M	223·25	946·5	+324%
Mean increase after O.B.E.				264%

TABLE II.—*Effect of Castor Oil*

Case No.	Gravidity	Index of Contractile Work of Uterus		
		Before Castor Oil	After Castor Oil	Increase after Oil
16	P	603·0	1,070·0	+78%
17	M	70·0	212·75	+204%
18	M	550·5	1,120·5	+104%
19	M	404·5	631·5	+56%
20	M	183·0	730·25	+299%
21	P	1,242·25	1,060·75	−15%
22	P	656·5	1,661·0	+153%
23	P	409·0	1,122·25	+174%
24	P	555·25	690·5	+24%
25	M	426·5	2,134·75	+401%
26	P	514·75	471·5	−8%
27	M	58·5	644·0	+1,001%
28	P	120·0	269·5	+125%
29	M	441·25	825·0	+87%
30	P	487·5	1,028·75	+111%
Mean increase after oil				186%

TABLE III.—*Effect of Enema*

Case No.	Gravidity	Index of Contractile Work of Uterus		
		Before Soap Enema	After Soap Enema	Increase after Soap Enema
31	M	139·25	258·0	+85%
32	M	327·5	526·0	+60%
33	P	1,324·0	1,054·75	−20%
34	M	148·25	269·75	+82%
35	P	252·5	522·0	+107%
36	P	112·5	159·5	+42%
37	M	243·5	521·5	+114%
38	P	476·0	438·0	−8%
39	M	180·0	228·25	+27%
40	P	41·25	245·5	+495%
41	P	122·75	215·0	+75%
42	M	764·25	871·5	+14%
43	P	277·0	446·75	+61%
44	M	199·25	571·25	+187%
45	M	364·25	761·0	+109%
Mean % increase after soap enema				95%

Table I shows that the administration of an O.B.E. increases the contractile work done by the uterus by an average of 264%. In this series of percentage increases the standard error is 51.6, and the mean of +264% is significant ($P<0.001$). A typical tracing of the effect of an O.B.E. is shown in Fig. 1, a.

Table II shows that the administration of castor oil alone increases the contractile work done by the uterus by an average of 186%. In this series of percentage differences the standard error is 64.9, and the mean of +186% is significant ($P<0.02$ but >0.01). A typical tracing of the effect of castor oil is shown in Fig. 1, b.

Table III shows that the administration of a soap enema alone increases the contractile work done by the uterus by an average of 95%. In this series of percentage differences the standard error is 31.6, and the mean of +95% is significant ($P<0.01$ but >0.001). A typical tracing of the effect of a soap enema is shown in Fig. 1, c.

Table IV shows that the administration of a hot bath alone has little effect on the contractile work done by the uterus. In this series of percentage differences the standard error is 3.6, and the mean of +6% is not statistically significant. A typical tracing of the effect of a hot bath is shown in Fig. 1, d.

TABLE IV.—*Effect of Hot Bath*

Case No.	Gravidity	Index of Contractile Work of Uterus		
		Before Hot Bath	After Hot Bath	Increase after Hot Bath
46	P	27·5	28·0	+2%
47	P	154·5	139·0	−10%
48	P	82·5	110·0	+33%
49	P	96·0	94·0	−2%
50	P	0·0	0·0	0%
51	P	345·75	431·5	+25%
52	M	293·5	302·5	+3%
53	P	193·0	173·0	−10%
54	M	312·75	284·5	−9%
55	M	272·5	313·25	+15%
56	M	194·25	198·25	+2%
57	M	89·0	95·25	+7%
58	M	227·5	273·0	+20%
59	M	132·75	146·0	+10%
60	M	169·0	163·75	−3%
Mean increase after hot bath				6%

TABLE V.—*Control Group*

Case No.	Gravidity	Index of Contractile Work of Uterus		
		First Tracing	Second Tracing	Percentage Difference
61	P	288·75	268·5	−7%
62	P	1,057·75	1,166·0	+10%
63	M	126·0	103·5	−18%
64	P	547·5	481·5	−12%
65	M	337·5	273·5	−19%
66	P	75·0	91·5	+22%
67	P	145·0	153·5	+6%
68	M	241·25	231·0	−4%
69	P	98·0	101·0	+3%
70	M	852·0	705·0	−17%
71	P	209·0	231·75	+11%
72	M	46·0	40·0	−13%
73	M	199·5	136·5	−32%
74	M	183·25	198·0	+8%
75	P	231·5	250·75	+8%
Mean difference				−4%

Table V shows that in the control group there is a spontaneous variation of uterine activity in these individual cases between −32% and +22% in the course of three hours. In this series of percentage differences the standard error is 3.8, and the mean of −4% is not statistically significant.

It can be concluded, therefore, that in the groups given an O.B.E., castor oil, a soap enema, or a hot bath any significant change in uterine activity can be attributed directly to the treatment.

Discussion

Consideration of the results described shows that the administration of castor oil, a soap enema, and a hot bath to a woman between 38 and 41 weeks pregnant causes a marked increase (264%) in the contractile work done by the uterus. The most effective component is castor oil (+186%). A soap enema produces a less marked but still considerable effect (+95%), while a hot bath produces no change of statistical significance (+6%). Castor oil and a soap enema, therefore, probably

act synergistically to produce the full effect of a complete O.B.E., the hot bath playing little or no part.

According to Reynolds *et al.* (1954) there is a direct relationship between the intensity of uterine activity in the later weeks of pregnancy and the time of onset of labour: the greater the uterine activity the earlier labour begins. Therefore, as the work done by the uterus is increased by the administration of an O.B.E., it seems highly probable that this procedure will often expedite the spontaneous onset of labour or, alternatively, increase the effectiveness of other methods of induction, such as artificial rupture of the membranes.

It is possible that another more palatable purgative could be proved to have the same oxytocic activity as castor oil.

Summary

The effect of castor oil, a soap enema, and a hot bath (a complete O.B.E.) and its individual components on the activity of the pregnant human uterus near term has been studied, using the guard-ring tocodynamometer.

The marked increase in uterine activity produced by an O.B.E. justifies its retention in obstetric practice as a method of induction of labour or as a prelude to other induction procedures.

A hot bath, while not contributing to this response, has other obvious effects which favour its continued use.

We thank Professor J. C. McClure Browne and Professor Norman Morris for their help and encouragement in the preparation of this paper. Thanks are also due to the sisters and nursing staff of the antenatal ward for their co-operation at all times.

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A HAND-OPERATED RESUSCITATOR

BY

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In the first-aid treatment of respiratory failure from any cause, speed in applying artificial respiration is essential. Any form of ventilation, whether manual or otherwise, may be life-saving if it is applied at once, and there is a growing view that positive pressure, either in the form of mouth-to-mouth or by machine, is more effective Possibly because of aesthetic considerations, the mouth-to-mouth method has never achieved the popularity it deserves, and, although many positive-pressure machines are now available, most of them can be operated only by trained medical personnel, and are complicated and cumbersome because they need oxygen cylinders.

The ideal machine should be simple, portable, and robust; cheap to manufacture so that it can be available in large numbers; and designed in such a way that it can be used by untrained personnel. A simple hand-operated resuscitator, which appears to meet all these requirements, has been developed by the Ministry of Supply.

It consists of three main components: (1) rubber facepiece, (2) exhalation valve unit, and (3) air supply unit (Fig. 1). All the metal parts are anodized aluminium, and all the rubber parts are of high quality, with a life of at least ten years. The components are connected together by simple screwed joints, so that they can be disconnected for cleaning. The whole apparatus can be sterilized by autoclaving or by boiling.

The Apparatus

Rubber Facepiece.—This consists of a rubber oro-nasal mask which has been specially designed for the resuscitator to meet the requirements of a close pressure-tight fit on as wide a range of faces as possible, coupled with support of the lower jaw. The fit on the face is achieved by a large anatomically shaped pneumatic cushion, which is formed integrally with the wall of the mask. This cushion is filled with air at atmospheric pressure, and can be opened and closed manually by means of a small knurled screw (not shown in Fig. 1), turning in a special metal pressure-release plug situated on the left cheek of the mask. This enables the air in the cushion to be maintained at atmospheric pressure, and provides a means of venting the cushion during sterilization of the facepiece. Attached to the front of the mask is a female screw adapter which is so positioned that when the facepiece is connected to the rest of the apparatus it is at the correct angle to thrust the patient's jaw upwards when the bellows are operated, thus ensuring a clear airway (Fig. 2).

Exhalation Valve Unit.—The valve is a slightly concave, moulded rubber diaphragm with a central circular orifice which is closed by a hinged rubber flap. In its resting position, the diaphragm is lightly pressed against a circular metal seating on the bellows side of the unit. When the bellows are compressed the diaphragm is raised off its original seating by the air pressure and seals against a larger circular seating on the facepiece side of the unit, and air passes through the central orifice into the facepiece. At the end of the compression stroke the valve returns to its resting position and the patient exhales freely to atmosphere through a gap around the periphery of the unit. The hinged flap over the central orifice in the diaphragm ensures that the air will not leak back past the diaphragm, and thus that no exhaled air can be drawn into the bellows. The flap is reinforced by a slightly larger disk of rubber riveted to it to prevent it from becoming inverted irreversibly. The diaphragm valve is contained in a flat circular metal housing, which has a male screw adapter at one side and a female screw adapter at the other, which prevents the unit from being assembled in the resuscitator the wrong way round.

If necessary, for civil defence purposes an anti-gas canister can be fitted between the facepiece and the exhalation valve unit.

Air Supply Unit.—The unit consists of a circular rubber bellows, with a male screw adapter at one end for connexion to the exhalation valve unit. At the outer end of the bellows, mounted on a metal plate, are

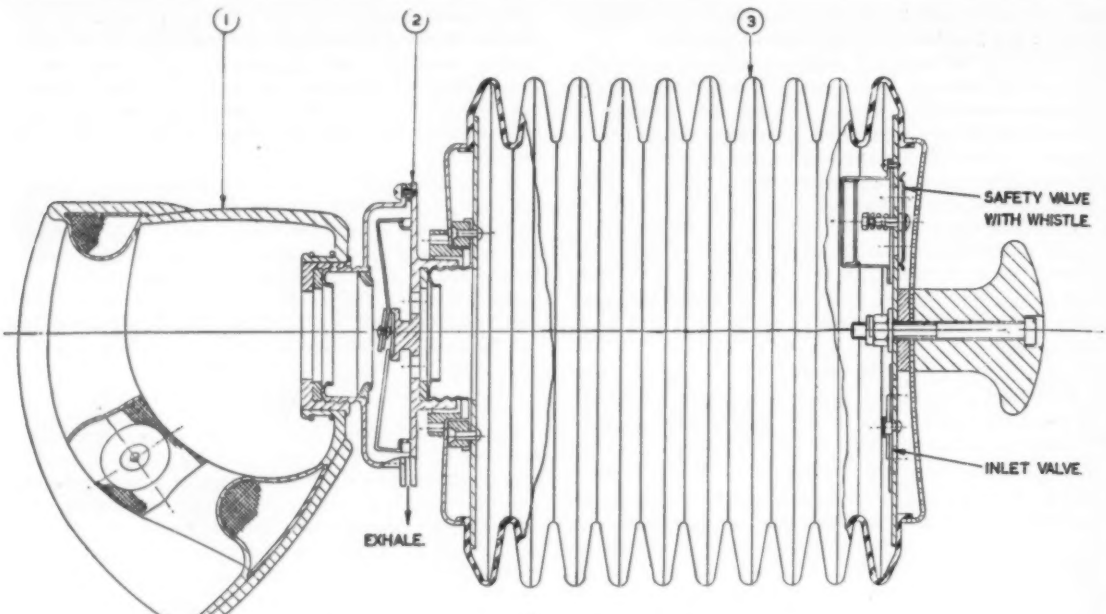

FIG. 1.—General arrangement diagram of the resuscitator.

(1) a knob handle for working the bellows; (2) a rubber disk inlet valve; and (3) a spring-loaded metal disk safety-valve, which is set to release at a pressure of 22 mm. Hg (30 cm. H_2O) to prevent over-inflation of the lungs. Incorporated in the safety-valve is a whistle to give audible warning that the patient is being ventilated too vigorously or that air is not reaching the lungs. When used for resuscitation the bellows will deliver approximately 2.5 litres per stroke.

Application of the Resuscitator

The whole apparatus weighs just under 2 lb. (0.9 kg.) and is contained in a rigid box, 10 by 6 by 6 in. (25 by 15 by 15 cm.), with a carrying-handle. Inside the lid of the box are the following instructions for use of the device.

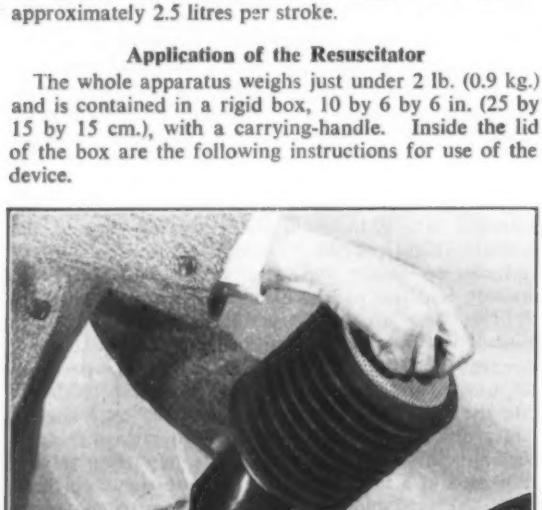

FIG. 2.—Resuscitator in use.

1. Place the mask firmly on the patient's face with the lower rim under the chin and the upper rim as high on the bridge of the nose as possible.

2. Work the bellows steadily at about 16 strokes a minute. The thrust of the bellows should be upwards on the face, so that the jaw is kept up.

3. Watch the chest. It should rise with each down stroke of the bellows, and fall during each up stroke. *If the chest does not rise and fall—First* make sure that the mask is tight on the face. *Then* listen to the bellows during the down stroke. If a whistling noise is heard the patient's throat is blocked and must be cleared. Insert a finger, covered with a handkerchief, down his throat to remove mucus or other obstruction. *If the chest rises and falls* and the whistle is heard, the pumping is too vigorous. Reduce the force being used.

4. Continue resuscitation until the patient breathes naturally, or for at least two hours.

Comment

This device has been thoroughly tested during the past eight years, both experimentally and clinically, on a large number of unconscious subjects in Service and civilian hospitals under widely varying climatic conditions, from the Arctic to the tropics, and has been found to be entirely satisfactory. It has been used successfully on cases suffering from poliomyelitis being transported by air, for emergency resuscitation in hospital wards, and by hospital orderlies previously untrained in its use. It has also formed part of a controlled study on artificial respiration (Lucas and Whitcher, 1958).

The design of the resuscitator has been developed at the Chemical Defence Experimental Establishment under the general direction of one of us (C. G. T.), but the details are due to a number of past and present members of the staff of that establishment.

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Medical Memoranda

Subserous Jejunal Haemorrhages During Mecamylamine Therapy

In the treatment of hypertension with ganglionic blocking agents, one of the most frequent complications is constipation. This may progress to a paralytic ileus if not dealt with immediately, and can present as an acute abdominal emergency. Bourne and Hosford (1951) describe a case which was operated upon during hexamethonium bromide therapy, when the findings at laparotomy were a grossly distended oedematous small bowel, with no evidence of mechanical obstruction. Similar cases have been described by Goldstone (1952) and McCalla *et al.* (1953), where again the operative findings were simply small-bowel distension with no obvious cause of obstruction. Grant and Boyd (1957) reported a case of ileus due to mecamylamine ("inversine"), where the small bowel was distended and no tumour or cause of obstruction was found. The following is the description of a case of hypertension on treatment with mecamylamine, presenting as an acute abdominal emergency in which the jejunum showed subserous haemorrhages.

CASE REPORT

A head mistress aged 42 was admitted to hospital on December 13, 1957, as an acute surgical emergency. She complained of severe, generalized, colicky abdominal pain of 18 hours' duration, which did not radiate through to the back. She had vomited many times, the material being food and bile at first, becoming brown and offensive later. Her bowels had been opened normally two days previously, and micturition was normal.

Twenty-two years ago she had had an appendicectomy for acute appendicitis with peritonitis. Since March, 1956, she had been under the care of one of us (J. R. H. T.) for hypertension, and had been having mecamylamine for just over a year. At the time of admission she had been taking mecamylamine, 10 mg. t.d.s., and "raudixin," 50 mg. t.d.s., for two months.

On examination she was pale and nervous, and was having severe abdominal pain. Her pulse rate was 100, temperature 99.2° F. (37.3° C.), and blood pressure 190/135 mm. Hg. The abdomen was slightly distended, with generalized tenderness and rebound tenderness to the left of the umbilicus. Rectal examination revealed tenderness in the pouch of Douglas. A plain vertical film of the abdomen showed some small-bowel fluid levels and a distended loop of jejunum to the left of the midline (Fig. 1). A diagnosis of "mecamylamine ileus" was made, so her stomach was aspirated hourly through an oesophageal tube, and she was given 5% glucose in normal saline intravenously.

Six hours later the pain and tenderness were still present, and, in view of the previous operation and the possibility of a strangulated loop of small bowel as the cause of the condition, a laparotomy was carried out.

Operation.—The abdomen was explored through a right central paramedian incision. The peritoneal cavity contained a moderate amount of pale-yellow clear fluid. There was no evidence of intestinal obstruction in either the small or the large bowel. In the lower jejunum about 3 ft. (90 cm.) of the small bowel was very noticeably covered with numerous bright-red subserous haemorrhages (Fig. 2). The affected bowel was not distended and only slightly thickened, there being no palpable mesenteric glands. This being the only abnormal finding, the abdomen was closed in layers.

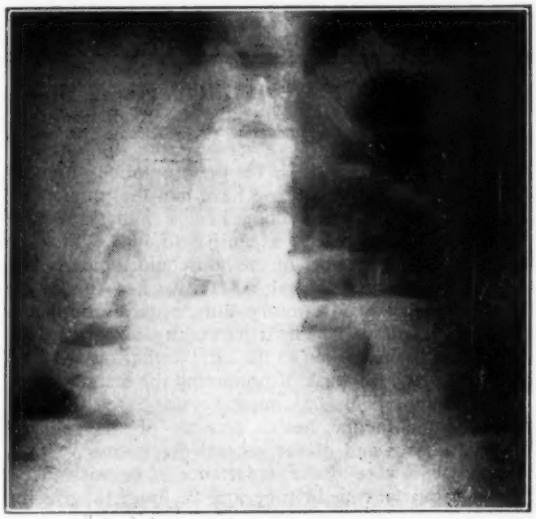

FIG. 1.—Plain vertical radiograph of the abdomen, showing small-bowel fluid levels and distended loop of jejunum.

FIG. 2.—Photograph of affected loop of jejunum at operation, showing subserous jejunal haemorrhages.

Post-operative examination of the blood showed a normal count, clotting-time, and bleeding-time; the platelet count was 169,000, with normal platelet morphology.

The patient made an uneventful recovery and was discharged home 10 days later.

We thank Mr. A. L. Pegg for the illustrations.

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Reviews

PSYCHIATRY AND PUBLIC HEALTH

Psychiatry and Public Health. By G. R. Hargreaves. (Pp. 118. 12s. 6d.) London, New York, Toronto: Oxford University Press. 1958.

Since 1948 those responsible for the promotion of health and the prevention of disease have had the problem of mental health at their door like a hungry wolf—impossible to ignore but expensive to feed. That he must be made a member of the household is clearly laid down in the National Health Act. To find the means of interpreting this statutory duty requires no small effort of imagination. The tripartite organization of the health services has given to the local authorities a major part in the inspiring task of promoting the mental health of the nation. This task must be integrated with the work of the mental health services of the regional hospital boards and of the general practitioner, who is usually well aware of the importance of neurosis in his practice, but lacking in time and facilities to give the sort of psychiatric first aid which he alone can give. For this task the average medical officer of health has had virtually no training at all. Such advice as is available to him locally may come either from those whose experience has been mainly with severe mental disorder or from those in whom belief in psychopathological dogma is matched by inexperience of the common man and his ways. He thus has great difficulty in finding a vantage point from which he can take an administrator's view of the problems of mental health, of the patchwork of developing mental health services, of how they came into existence, and of how they can be made economical and effective in the future.

Professor Hargreaves's experience of mental health services throughout the world is unique, and while at W.H.O. he probably met more experts in this field and listened to more points of view than anyone alive. His own experience in industrial and military mental hygiene, together with his use of the historical approach, has enabled him to give the background and the present status of just those mental health problems that preventive medicine is striving to understand. In the first three of his Heath Clark lectures he traces the origins of psychiatry, its relation to society, and its special problems for medical administration. In the last two he deserts the historian's role for an interpretation of the present situation, and gives his own suggestions on the part which might be played by the family doctor and the mental health services. This is likely to be of greater use to the harassed M.O.H. than the slogans and single-minded approaches which he is apt to pick up from conference rhetoric. Even if experts in the different branches of psychological medicine may disagree with Professor Hargreaves about the probable causation of schizophrenia, for instance, or the importance of emotional deprivation in early life, this should not detract from the value of a book which is not to be read for its facts but for the ideas which it makes available in a brief and readable form that calls for no psychiatric sophistication. General practitioners and medical officers of health may well be stimulated, after this general guide, to seek further detail in some of the fields touched upon, and a short bibliography and guide to further reading on the general principles underlying mental hygiene might have been a helpful addendum.

ALEXANDER KENNEDY.

HUMAN BIOCHEMISTRY

Human Biochemistry. By Israel S. Kleiner, Ph.D., and James M. Orten, Ph.D. Fifth edition. (Pp. 808; illustrated. 67s. 6d.) London: Henry Kimpton. 1958.

The fifth edition of this well-established textbook appears four years after the last one, and Dr. I. S. Kleiner is now joined by Dr. J. M. Orten as co-author. The style and objectives of the earlier editions have been retained, but considerable sections have necessarily been revised. In particular the chapters on metabolism and on blood have been completely rewritten and many of the illustrations replaced by new ones. For those who wish to read further in any particular aspect of the subject general and special references to relevant selected papers are given at the end of each chapter.

The authors set out to produce a volume suitable and useful for students of medicine, dentistry, and related subjects, and they say that in the past *Human Biochemistry* "has also proved to be of considerable value as a ready 'refresher course' for clinicians." They do not include too much theoretical discussion or controversial material, but attempt to give the essence of the subject under discussion in a straightforward manner. For example, in rather less than two pages in the section on proteins Sanger's work on the structure of insulin is outlined and the structure of the molecule of insulin given: references to the literature allow those who wish to know more to acquire all the detailed information which they could need about this important work, which recently gained the award of the Nobel Prize in Chemistry. In the last chapter, entitled "Recent Clinical Applications," sections are devoted to liver- and kidney-function tests, blood pressure, psychopharmacology, dental caries, biochemistry of inflammation, biochemistry of tumours, chemistry of tumour tissue, acid phosphatase and the prostate gland, antibiotics, sulphonamide drugs, radioactive isotopes, enzymes and enzyme inhibitors, cortisone and corticotrophin in rheumatoid arthritis, and pyrogens. Appended to this chapter are 88 references to the original literature which open the door to a very wide vista of biochemistry in modern medicine.

F. G. YOUNG.

ONE-MAN TEXTBOOK

Text-book of Surgery. By Patrick Kiely, B.Sc., M.D., M.Ch.(N.U.I.), F.R.C.S.(Eng.). Second edition. (Pp. 1,158; illustrated. 63s.) London: H. K. Lewis and Co. Ltd. 1958.

In this second edition the author has excluded anaesthetics and gynaecology, but still retains 50 pages on diseases of the eye. The sections dealing with diseases of the nose, throat, ear, and eye are written by Professor O'Hea Cussen. All the rest is from the pen of Professor Kiely, who has succeeded in presenting the main facts of surgery within reasonable compass. For a textbook it is also well up to date, though there is still in some parts a tendency to cling to the older outlook. The pattern of surgery has changed rapidly during the past 20 years. A generation ago tuberculous arthritis and the gummatous lesions of syphilis were common, but to-day the one is rapidly diminishing and the other is seldom seen. Perhaps textbooks cannot change so rapidly, because some examiners are conservative in outlook.

In the section on burns we should like to see some indication of how much plasma should be given for any particular burn, and the urgency of its administration

pointed out. It might also be mentioned that there have been successful resections of aneurysms of the aorta well above the origin of the inferior mesenteric artery.

One advantage of a "one-man" textbook is that a personal note may sometimes lighten the page, as when the author of this book mentions that he himself has an unstable lower end of the ulna following a Colles fracture. The type is clear and the publishers have produced the book well.

ZACHARY COPE.

ADVANCES IN PAEDIATRICS

Advances in Pediatrics. Edited by S. Z. Levine. Volume X. (Pp. 362; illustrated. 67s.) Chicago: Year Book Publishers, Inc. London: Interscience Publishers, Ltd. 1958.

The tenth volume of *Advances in Pediatrics*, under the skilled editorship of Dr. S. Z. Levine, contains seven critical reviews of current topics and is well up to the standard of its predecessors. It is difficult to review without giving a short catalogue of contents. The treatment of tuberculosis in childhood (Edith Lincoln), convulsive disorders (S. Livingstone), poliomyelitis vaccines (A. B. Sabin), and staphylococcal infections in nurseries (by a team of three) all deal with important aspects of current work among children. Growing interest in muscular disorders is reflected in a chapter by F. H. Tyler; and from a non-American source comes a thoughtful article on the transfer of antibodies from mother to offspring by B. Vahlquist, of Uppsala. Quite the most outstanding article even against the high level of other contributors, however, is by Barbara M. Korsch on the present-day psychological principles which lie behind paediatric work. Her final summing-up, answering the question, "What can the physician do?" contains a wealth of good advice in under six pages.

ALAN MONCRIEFF.

DERMATOLOGY FOR NURSES

The Nursing and Management of Skin Diseases. By D. S. Wilkinson, M.D., M.R.C.P. (Pp. 288; illustrated. 32s. 6d.) London: Faber and Faber. 1958.

This book will prove attractive because of its freshness of approach and of a style which is easy without being slipshod or colloquial: nurses, for whom it is primarily intended, will find it interesting as well as informative.

Such a work as this must be reasonably brief. It is perhaps more difficult for the author to decide what to leave out than what to put in, and, as a result, he tends to include too much. It is, for example, doubtful whether the nurse will be much helped by the inclusion of 50 formulae for local applications, by details of the furniture required for an out-patient department, or by the table of hypnotics. In these and other ways there is an emphasis which often seems misplaced, but this perhaps is because the author also intends that the book should be used by general practitioners.

Good nursing is important in the treatment of many skin diseases, but it is inevitable that many nurses during their training will have no practical experience. This book will certainly help to supply the need, for in addition to ideas it contains much detailed, down-to-earth, and specific instruction on nursing procedure. Most of the illustrations are good; there are both photographs and line drawings of the acarus, *Phthirus pubis*, and nits, which hardly need to be duplicated in this way.

F. RAY BETTLEY.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Eisenstoffwechsel. Beiträge zur Forschung und Klinik. Edited by W. Keiderling. (Pp. 294; illustrated. DM. 48.) Stuttgart: Georg Thieme Verlag. 1959.

Nutrition and Atherosclerosis. By Louis N. Katz, M.D., Jeremiah Stamler, M.D., and Ruth Pick, M.D. (Pp. 146; illustrated. 37s. 6d.) London: Henry Kimpton. 1959.

Elements of Vital Statistics. By B. Benjamin, B.Sc., Ph.D., F.I.A., F.S.S. (Pp. 352. 56s.) London: George Allen and Unwin Ltd. 1959.

New and Nonofficial Drugs, containing Descriptions of Therapeutic, Prophylactic and Diagnostic Agents evaluated by the Council on Drugs of the American Medical Association, 1959. (Pp. 687+xxvii. 30s.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1959

Nourishing Brain Cells. An Inaugural Lecture. By C. E. Lumsden, M.D. (Pp. 23; illustrated. 2s. 6d.) Leeds: University Press. 1959.

Annual Volume of Physiology and Experimental Medical Sciences. First Issue (1957-58). Edited by Dr. S. R. Mukherjee, assisted by Dr. A. Bagchi and Dr B. Roy. (Pp. 137+ix; illustrated 20 rupees.) Calcutta. 1958.

Pregnancy, Birth and Abortion. By Paul H. Gebhard, Wardell B. Pomeroy, Clyde E. Martin, and Cornelia V. Christenson. (Pp. 282+xiii. 30s.) London: William Heinemann (Medical Books) Ltd. 1959.

Surgical Technique. By Stephen Power, M.S., F.R.C.S. Second edition. (Pp. 411+x; illustrated. 40s.) London: William Heinemann (Medical Books) Ltd. 1959.

Enuresis or Bed-wetting. By Franklin Bicknell, D.M.(Oxon.). With a foreword by J. Johnston Abraham, C.B.E., M.D., F.R.C.S. (Pp. 104. 7s. 6d.) London: William Heinemann (Medical Books) Ltd. 1959.

Understanding the Child. Habit Training and Bedwetting. By Sister Mary Martin, S.R.N., S.C.M. (Pp. 32. 1s.) London: Delisle Limited. 1959.

Essentials of Human Reproduction. Clinical Aspects, Normal and Abnormal. Edited by Joseph Thomas Velardo. (Pp. 270; illustrated. £5 10s.) New York: Oxford University Press. 1958.

Trends in Genetic Analysis. By G. Pontecorvo, F.R.S. (Pp. 145+x; illustrated. 25s.) New York: Columbia University Press. London: Oxford University Press. 1959.

T. H. Huxley, Scientist, Humanist and Educator. By Cyril Bibby. (Pp. 330+xxi; illustrated. 25s.) London: Watts. 1959.

Dangerous Marine Animals. By Bruce W. Halstead, M.D. (Pp. 146+v; illustrated. 30s.) Cambridge, Maryland: Cornell Maritime Press. London: Putnam and Co. 1959.

Orthopaedic Surgery. By Sir Walter Mercer, M.B., Ch.B. (Edin.), M.Ch.Orth.(Liv.) (Hon.), F.R.C.S.(Edin.), F.A.C.S.(Hon.), F.R.C.S.(Eng.) (Hon.), F.C.S.So.Af.(Hon.), F.R.C.S.I.(Hon.), F.R.S.(Edin.). 5th ed. (Pp. 1,075+xi; illustrated. 90s.) London: Edward Arnold (Publishers) Ltd. 1959.

Laparoscopia e Laparografia nella Pratica Medica. By Franco Bertolani. (Pp. 222; illustrated. L. 3,500.) Turin: Edizioni Minerva Medica. 1958.

Actions and Uses of Drugs. By Norman Sapeika, B.A., M.D., Ph.D.(Cape Town), F.R.S.S.Af. (Pp. 389. £3.) Cape Town, Amsterdam: A. A. Balkema. 1959.

Diseases of Laboratory Primates. By Theodore C. Ruch, Ph.D. (Pp. 600+xxvi; illustrated. 52s. 6d.) Philadelphia, London: W. B. Saunders Company. 1959.

Dreaming. By Norman Malcolm. (Pp. 128+vii. 12s. 6d.) London: Routledge and Kegan Paul. New York: Humanities Press. 1959.

What is Cybernetics? By G. T. Guilbaud. (Pp. 126+viii. 10s. 6d.) London: Heinemann. 1959.

Fat-free Cookery. By Alice Record Hooper. (Pp. 112+vi. 12s. 6d.) London: Oxford University Press. 1959.

Hunger and Food. Special edition of Science and Mankind. Edited by Professor Josué de Castro. (Pp. 123. 10s.) London: World Federation of Scientific Workers. 1958.

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MEDICAL ETHICS

> "There is a certain aura about any professional man, whether he be doctor, lawyer, or dental chief. Perhaps it is the strictness of the code of ethics under which he works which gives him an authority denied to other men."

The *Manchester Guardian*, from which this quotation comes, might have added that without a strict code of ethics and a high standard of education medical practitioners would have no claim to professional status. Each country has its ethical rules. What distinguishes England to-day is the way the rules are flouted, and the apparent indifference to this of the General Medical Council. In the excellent weekly French illustrated journal *Paris-Match* there appeared in one of its February numbers an account of recent work on leukaemia and injections of bone marrow. In this account, which by British standards was restrained and well-informed, there was a photograph of the head of Professor Mathé, whose work, among others, was discussed in the article. At the beginning of April *Paris-Match* published a letter from Professor Mathé which began by saying that he was professionally disturbed to see a photograph of himself, and the article, in that journal. He insisted that he had given neither the photograph nor an interview to *Paris-Match*, and he requested them to publish this letter of protest "conformément à la loi." In a fairly lengthy editorial comment, *Paris-Match* said they knew the Ordre des Médecins forbade all publicity to its members—and then went on to say that nevertheless they felt it their duty to let their readers know of work which brought such great credit to French medicine.

We wish British doctors would take a lesson from this French example rather than cast their eyes on what they believe to be the publicity methods of our colleagues in the U.S.A., which, when they imitate them, they imitate so clumsily, if only because this sort of thing does not suit the British character and temperament. Not so long ago someone observed that one of the first casualties of the National Health Service was medical ethics, an observation that has been made by many others, though not so neatly. The worst offenders seem to be surgeons and psychiatrists (including hypnotists). Some time between July, 1948, and now a president of one of our famous national institutions, to celebrate his election to that office, gave an interview to a journalist, and his life story was entertainingly told in one of the national newspapers, along with the inevitable photograph. We believe he was then still in active practice, but do not recall having seen any such subsequent letter of protest as has characterized the more modest Professor Mathé, of Paris. Psychiatrists and medical hypnotists have had bits of their books reproduced in evening papers, so laid out by the sub-editors to look as if they were articles written especially for those papers. A psychiatrist wrote a series of essays for a Sunday newspaper—anonymously—and then the game was given away when they were published shortly afterwards under his own name in book form.

The existing confusion of standards is illustrated by a recent letter in the *Daily Telegraph*: "On April 16 we had the spectacle of seeing . . . introduced by name (and quite rightly, too) for his afternoon talk [on a television programme] on plastic surgery. But in the evening programme 'Life Line' the psychiatrist was anonymous 'because he was a doctor.'" The correspondent began by saying that it was surely time that consistency was brought into the question of giving the names of doctors appearing on television. We agree. The medical profession in this country should make up its mind whether or not it is going to behave like a profession by following a code of ethics which is by no means strict and is based really more on the principles of common decency than on legal ruling. The consistency, in other words, must come from the profession and not from the press or the broadcasting and television authorities. The President of the National Union of Journalists said at a meeting on April 23: "In the mad race for newspaper circulation, sensationalism ranks higher than service to the public." And as part of this the press has been working hard, along with the broadcasting authorities, to break down the traditional medical reserve. They have succeeded to such an extent that if we are really to be honest with ourselves we had better tear up our code of ethics and admit without pretence that the discretion and decorum that have been a traditional aspect of doctors' behaviour for centuries are now in the discard.

Let us take the question of television and anonymity. Doctors appear under their names on the television screen. The G.M.C. has not officially changed its opinion, given in a resolution in 1934,

"that it is desirable, in the public interest, that registered medical practitioners should broadcast anonymously." (This was not well put, but it meant that if doctors did broadcast they should remain anonymous.) In 1951 the B.M.A.'s Representative Body resolved that "practitioners approached to appear in such programmes [of public education on selected health matters], whether for 'sound' or 'visual' broadcasting, should insist on anonymity as part of the contract." In 1955 the Independent Television Authority undertook to bring the B.M.A.'s report on indirect methods of advertising and its policy of anonymity to the attention of companies providing programmes. The B.M.A. has stated that a practitioner's photograph appearing in the lay press in connexion with an interview or an article on professional subjects "is a most undesirable form of publicity." It added that "every reasonable precaution should be taken that such photographs are not published." In the Notice[1] issued by the Disciplinary Committee of the G.M.C. under the heading of "Advertising and Canvassing" is a reference to the "procuring, or sanctioning, or acquiescing in the publication of notices commending or directing attention to the practitioner's professional skill, knowledge, services, or qualifications. . . ."

These statements by the G.M.C. and the B.M.A. are being increasingly ignored, and at times, we regret to say, by those whose very seniority and position should impose on them a scrupulous care for etiquette and ethics, because if they do not pay any attention to them how can they expect their younger colleagues to do so? *Noblesse oblige*. The present growing and almost contemptuous disregard by not a few of our profession for ethical codes which, after all, have been arrived at with care and thought, is bringing discredit to the profession, and will add up to create one more cause for the public to suspect the doctor of being a bit of a hypocrite. If those responsible for framing ethical codes and for seeing that they are respected have come to the conclusion that a decline of standards is inevitable in the N.H.S. and in a world of "soft advertising," they had better roundly say so and let those who hunger and thirst for publicity have their fill. What is doing the profession no good in the eyes of itself or in the eyes of the public is a lip service to certain canons of good taste and professional ethics, and a behaviour that runs exactly contrary to what it says. It is indeed time that some consistency was brought into this matter, if only for the reason that, as the *Manchester Guardian* hints, it is a strict code of ethics principally which distinguishes a profession from a trade.

[1] *Yearbook 1958-59*. British Medical Association. November, 1958.

COLLEGE OF PATHOLOGISTS

The Association of Clinical Pathologists has recently circularized its members asking them whether or not they favour the establishment of a college of pathologists. We understand that some 75% are in favour. The association will probably by now have received most of the replies to a similar inquiry made among pathologists who are not members of the A.C.P. but members, in all probability, of the Pathological Society of Great Britain. It is safe to assume that a majority of the latter will also support the majority of the Association of Clinical Pathologists.

For a long time now there have been rumours of discontent among pathologists about their status and about their relationship to the Royal College of Physicians of London. As pathology is the basic clinical science, indispensable to the practice of medicine, surgery, obstetrics, and gynaecology, it is indeed remarkable that, following the traditional professional pattern, pathologists have not staked out a claim for a college sooner than this. Or, to put it another way, if any discipline of medicine deserved to be recognized through the setting up of some institution, then pathology would have the highest claim, certainly now in this twentieth century of scientific medicine. The clinical pathologist is an indispensable and, more often than not, a key figure in the medical or surgical team now playing such an outstanding part in the development of modern medical and surgical science. If status, prestige, influence, preservation of standards, academic progress all tend to be enhanced by a college representing a clear-cut discipline within Medicine, then the claims of the pathologists to set up a national institution to enshrine all these things cannot be gainsaid. Pathologists here have no doubt noted that the College of Pathologists of Australia was established in 1956, the inaugural meeting being held in the hall of the Royal Australasian College of Surgeons.

In Britain pathologists have looked rather towards the Royal College of Physicians of London, though not always with a friendly glance. Some pathologists have acquired the M.R.C.P. on the strength of published papers. Others have had to jump the difficult hurdle of the M.R.C.P. examination, and as pathologists some have regretted the time spent on this arduous clinical exercise. Some have become Fellows of the College by ordinary or by special election. It might be possible, by an adjustment of the constitution, to bring the pathologists within the fold of the College of Physicians, and so avoid the

establishment of yet another institution and an apparent division in medicine itself. But such a move might eventually turn out to benefit neither of the two principal components of what the future College would thus become. In any new college of pathologists, it is thought that between 500 and 1,000 would fairly soon have a title to be recognized as fellows. If this is correct, and if they were all part of the one College of Physicians, then pathologists as F.R.C.P.s would in fact in time outnumber the F.R.C.P.s who were first and foremost practising clinicians. All sorts of internal rivalries and jealousies would arise, and there would be a scramble for the various offices on the part of those who were principally pathologists and of the others who were principally physicians. The College of Physicians has historically been—and in our view should continue to be—a College of Physicians who practise clinical medicine, with an odd assortment of other kinds of Fellows, such as administrators and medical editors, to set them off. The authority and influence of the College are based on the practice of clinical medicine.

No doubt the controversy on this problem will follow the pattern of such controversies, and a lot of manœuvring for position will take place. The establishment of a College of Pathologists might well turn out to be a stimulus to medicine and surgery. That a new college under wise and energetic direction can quickly become a force for good is shown by the brief but remarkable history of the College of General Practitioners. All clinical workers owe so much to their colleagues in pathology that they will watch the evolution of the present decision with warm sympathy.

POST-GASTRECTOMY SYNDROMES

Since the advent of gastric surgery towards the end of the nineteenth century, a new series of syndromes have been introduced. These syndromes are the result of resection of part of the stomach and of the consequent readjustment of the anatomy of the upper gastro-intestinal tract. In the opening pages of this issue Mr. Hermon Taylor relates the frequency and severity of the symptoms with the technique used in the operation. After resection of the stomach there are two methods of restoring the continuity of the gastro-intestinal tract. The gastro-duodenal anastomosis (Billroth I) is technically the simplest procedure, and the morbidity resulting from it is extremely low when compared with that of the gastro-jejunal anastomosis (Polya). The numerous syndromes range from post-prandial nausea, vomiting of food or bile, "dumping syndrome," uncomfortable distension of the abdomen, diarrhoea, and failure to gain weight to continuously failing nutrition, with its attendant physical and mental breakdown.

The cause of these post-gastrectomy syndromes can be grouped under two main headings—the anatomical and physiological disorientations. The greater the disorientation caused by surgery the greater will be the physiological disturbances, until a stage is reached when they become clinical entities. Surgical procedures which exclude the duodenum from the passage of food lead to a derangement of digestion and absorption by altering the time relationships between the secretion of gastro-intestinal juices—the hepatic, pancreatic, and small-intestinal secretions and the arrival of the food and the juices in the stomach remnant.

In gastroduodenal anastomoses the anatomical disturbance is minimal and consequently the physiological upsets are likewise minimal. The intestinal tract soon adjusts itself to the lack of a pylorus and to the presence of a small stomach which empties rapidly. Unfortunately this operation should not be performed on patients with duodenal ulceration because of the higher acid secretion of the gastric remnant. The failure to neutralize this acid by food leads to a high rate of recurrent ulceration at the gastroduodenal stoma.

After gastrojejunal anastomosis the duodenum is closed at its proximal end and therefore becomes no more than a continuation of the common bile duct and pancreatic duct. When the abnormal reservoir thus formed is associated with any degree of obstruction resulting from the operation, there may be such delay in the passage of hepatic and pancreatic secretions into the jejunum that they may never intermix with the chyme. This is particularly likely to happen when the gastric remnant empties within ten minutes of the intake of food. In other cases defects in the intermixing and subsequent digestion of the food lead to clinical symptoms of varying severity.

Duodenal distension and subsequent biliary stasis and pancreatic retention are the result of surgical strictures on the afferent side of the gastrojejunal stoma. Such strictures can occur in the standard antecolic or retrocolic operations, in which the small intestine must be taken above the transverse mesocolon. Such tension syndromes are minimal

1 Gilbert, J. A. L., and Dunlop, D. M., *Brit. med. J.*, 1947, **2**, 330.
2 Barnes, C. G., *Lancet*, 1947, **2**, 536.
3 Glaessner, C. L., *Rev. Gastroenterol.*, 1940, **7**, 528.
4 Hertz, A. F., *Proc. roy. Soc. Med.*, 1913, **6**, 155.
5 Mix, C. L., *Surg. Clin. N. Amer.*, 1922, **2**, 617.
6 Roberts, K. E., Randall, H. T., and Farr, H. W., *Surg. Forum*, 1954, **4**, 301.
7 Hoffmann, V., *Münch. med. Wschr.*, 1939, **86**, 332.
8 Smith, W. H., *Lancet*, 1951, **2**, 745.
9 Everson, T. C., *Surgery*, 1954, **36**, 525.
10 Henley, F. A., *Brit. J. Surg.*, 1952, **40**, 118.
11 —— *Ann. roy. Coll. Surg. Engl.*, 1953, **13**, 141.
12 —— *Med. Press*, 1955, **233**, 318.

when the gastrojejunal anastomosis is below the transverse mesocolon, as in the Finsterer modification of the Polya operation, and when the site of the anastomosis is as near as possible to the ligament of Treitz. This reduces to a minimum the amount of duodenum acting as a blind segment, and thus contributes to a more rapid emptying, with consequent improvement in physiological results.

The metabolic disturbances are greatest when a gastro-ileal anastomosis has been accidentally performed. Here there is incessant diarrhoea, with steatorrhoea, anaemia, and failure to maintain nutrition. The nearer the site of anastomosis to the duodenum the less the metabolic disturbance, and therefore any surgical procedure which attempts to place the anastomosis as high as possible in the jejunum and without any acute angulations of the gut will minimize post-gastrectomy morbidity. Mr. Hermon Taylor describes in his paper a technique which meets these criteria for a satisfactory operation.

The "dumping syndrome" may also be a physiological response of a particular patient to an anatomical disturbance of his upper gastro-intestinal tract, and is not necessarily dependent upon the particular type of operation performed. Its symptoms vary from flushing, a feeling of warmth, sweating, nausea, and palpitations to faintness and sometimes explosive diarrhoea. It may come on within fifteen minutes of a meal, and the patient may have to lie down to overcome the faintness. Several theories have been put forward to explain the dumping syndrome. J. A. L. Gilbert and D. M. Dunlop,[1] in 1947, showed that too rapid passage of the food into the jejunum resulted in an initial hyperglycaemia followed by a secondary hypoglycaemia. At the same time C. G. Barnes[2] also reported three cases of severe hypoglycaemia resulting from partial gastrectomy, and suggested that it was due to insulin sensitivity caused by repeated episodes of hyperglycaemia after the intake of food. This same suggestion was first made in 1940 by C. L. Glaessner,[3] who called the condition hyperglycaemic shock. An earlier theory was that the rapid emptying of the gastric remnant caused over-distension of the jejunum.[4]

C. L. Mix[5] added the word "dumping" to the description of the syndrome in 1922. Among other suggested causes are hypovolaemic shock due to osmotic inflow into the jejunum of plasma constituents,[6] and reflex pooling of blood in the splanchnic vascular bed due to too rapid entrance of food into the small intestine, with a consequent depletion of blood in the brain.[7] Hypopotassaemia has also been put forward as a possible cause,[8] and it may well be a combination of these various physiological changes that result in the dumping syndrome in any one individual. It is worth bearing in mind that in only 30–35% of patients are the symptoms severe enough to warrant medical or surgical treatment.

T. C. Everson[9] reported that between 16 and 75% of patients failed to gain weight after gastrectomy of the Polya type, and the metabolic studies he carried out on dogs clearly showed the physiological disturbances it caused. Excessive loss of weight can sometimes be prevented by avoiding extensive resection of the stomach in patients who had had difficulty in maintaining their weight pre-operatively. If, however, the loss of weight is associated with any of the post-gastrectomy syndromes, including stomal ulceration, surgical readjustment may be necessary by conversion of the Polya type operation to that of the Billroth I. The remedial operation of jejunal replacement[10–12] eliminates the severe post-gastrectomy syndromes and does not appear to result in recurrent ulceration, provided that the Polya gastrectomy has been present for at least six months. It should not, however, be performed if stomal ulceration is already present, or if the patient concerned will not, or cannot, conform to the dietetic regimen laid down by his medical advisers.

DANGEROUS TOYS

Surprisingly little is known about the causes of non-fatal accidents to children.[1] To help remedy this defect a committee of the Portsmouth Junior Chamber of Commerce carried out an inquiry recently into the hazards of toys. Their interesting report appeared last week,[2] and its main conclusion is that "a large proportion of children are faced with real danger at play."

Members of the committee filled in questionary forms to record information about children known to them. In this way they gathered data about 336 children and found that 138 (41%) of them had had accidents caused by toys. The ages of the children are not given in detail. These 138 children had had 209 accidents; of these accidents, 33 (16%) were classified as serious, and two more were fatal. In other words, about 10% of the children had suffered serious or fatal accidents due to toys. When the actual causes of the accidents were examined they were found—too often—to be the natural result of bad design in the toys. Mechanical toys with

[1] *Wld Hlth Org. techn. Rep. Ser.*, No. 118, Geneva, 1957.
[2] *Danger at Play*, Portsmouth Junior Chamber of Commerce, 46, Commercial Road, Portsmouth, 1959.
[3] Rowntree, G., *J. Hyg. (Lond.)*, 1950, **48**, 323.
[4] Burrows, N. F. E., Rendle-Short, J., and Hanna, D., *Brit. med. J.*, 1951, **1**, 329.
[5] Gibb, J. W. G., and MacMahon, J. F., ibid., 1955, **1**, 320.
[6] Marsdon, H. B., and Wilson, V. K., ibid., 1955, **1**, 324.
[7] Millichap, J. G., Llewellin, K. R., and Roxburgh, R. C., *Lancet*, 1952, **2**, 360.
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knife-sharp edges to the metal, highly inflammable celluloid, teddy-bears' eyes on sharp pins, lead in the paint on the toy or composing the material of which it is made—these were some of the commonest hazards. Too many toys had parts which could be, and were, detached and swallowed ; but though slipshod workmanship played some part in making toys unsafe it is evident that the main charge is of bad design. Again, some offensive weapons find their way into the hands of children as toys. This is notably true of flick-knives, and the attempt now being made to get them banned by law deserves every encouragement. Air-guns also cause serious harm on occasions, but this seems to be due to parental rather than legal laxity.

When considering how to prevent such accidents, there would seem to be a danger in laying too much emphasis on the psychology of the children who fall victim to them. The concept of the accident-prone person has sometimes been stretched far beyond the limits within which it can be a fruitful idea. No doubt some children are habitually more careless than others, and probably most are more careless when they are emotionally upset than when they are happy. But the first things here would seem to be to encourage the manufacture of safe toys and to encourage parents to choose with discrimination. This report serves a useful purpose in showing clearly that there is a need for action and in suggesting what features in the design of toys could be improved. Among the various causes of accidents among children,[5-10] badly designed toys may be more important than is generally known.

THYMOMA AND RED CELL APLASIA

Metaphysicians and others without direct experience of science or medicine usually believe that scientific method depends on induction—that is, the collection of innumerable examples from which a general law can be inferred. In practice, nothing could be further from the truth. Every observation causes the observer to generate innumerable hypotheses to "explain" the observation, and each hypothesis is tested against other experiences. A useful hypothesis is one which is contradicted by few experiences. Scientific "truth" is established when a hypothesis is found which conflicts with none or can be reconciled with all other experiences and observations.

Some recent reviews of aregenerative anaemia associated with thymoma[1-4] illustrate the uselessness of facts in science or medicine before the critical hypothesis on their relation is born in the mind of some observer, or before the critical observation generating it has been made. The reviews show that, out of 47 recorded cases of pure red cell aplasia, in 18 a thymic tumour has also been present. More than half of these cases have occurred in the United States during the last 15 years. Another case is now reported in this *Journal* at p. 1154 by Drs. E. H. O. Parry, G. S. Kilpatrick, and R. M. Hardisty. They found that thymectomy did not improve the aplasia but that normal erythropoiesis occurred later during treatment with prednisone. The patient died of staphylococcal septicaemia.

Pure red cell aplasia is a rare condition, and thymoma is not much commoner. They might by chance occur together in the same patient, but the reports of their doing so, though uncommon, seem frequent enough to suggest that the anaemia and the thymoma are in some way connected. When one asks how they are related, it is easy to generate hypotheses, but equally easy to show that each hypothesis is unsatisfactory. Some patients have been cured by thymectomy[5-7] and one by splenectomy, thymectomy, and administration of corticotrophin,[8] while another went into partial remission after thymectomy alone,[8] but others have not responded.[1 8-11] The attractive hypothesis that the tumour in some way causes the anaemia is thus disproved ; and the alternative, that the tumour cells generate an inhibitory factor or process which ultimately renders the hypoplasia irreversible, seems to be disproved by the case of a patient whose thymoma was resected two years before the anaemia developed.[1]

The only valid hypothesis at present seems to be that both tumour and anaemia are produced by something which has not yet been discovered, and that we await the clue which will guide us to this something. The disease is so rare that the wait promises to be long, but some encouragement may be derived from the surprising fruitfulness of the studies of A. S. Alving and his co-workers[12-20] on the anaemia produced by primaquine in about 10% of American Negroes. Hardly had they shown that the anaemia depended on a lack of glucose 6-phosphate dehydrogenase in the red cell than G. Sansone and colleagues[21-23] and A. Szeinberg and colleagues[24-26] showed that this same lack occurred in patients who developed haemolytic anaemias due to other drugs, and also in patients who suffered from favism ; and now it is known that the enzyme deficiency is inherited, apparently as a single factor with incomplete expression in the heterozygote.[27] The problem now is how such an odd anomaly became so widely distributed. Perhaps the peculiar association of anaemia and thymoma will be explained by studies in some apparently unrelated field.

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W.H.O. IN RESEARCH

Medical men are fortunate in that they are not fenced in by commercial or national secrecy. They publish and apply new knowledge as soon as they can, and, as Dr. M. G. Candau, director-general of the World Health Organization, said at its tenth anniversary last April,[1] "In the last ten years the flow and exchange of scientific information and practical experience have perhaps been greater than ever before." The W.H.O. has itself done much to help to spread medical knowledge quickly, as well as sending teams to apply it. In particular many tropical countries have cause to be grateful for the effective attack on parasitic diseases carried out by experts sent to them under the auspices of the Organization.

As well as undertaking field work to combat disease the W.H.O. has in the past encouraged a certain amount of research, notably by the setting up of special centres such as the influenza centre in London under Dr. C. H. Andrewes, F.R.S. Last year the Organization decided to extend its research activities, and the latest annual report[2] summarizes recent proposals. Its main concern, the W.H.O. considered, should be with "those problems which are better resolved by world co-operative endeavour than by local groups," and with those which are too much for particular local groups to tackle on their own. But the Organization intends to work through existing national institutions, not to set up independent or rival ones. The sort of studies it has in mind include the epidemiology of cancer, hypertension, coronary thrombosis, and rheumatoid arthritis; comparison of the effects of different environments on health and disease; and investigation of diseases so rare that cases from several countries must be collected to provide enough for fruitful analysis. In a world smouldering with hostility, it is pleasant that the director-general can conclude his preface to the report with these words: "It is most fortunate that this broadening of W.H.O.'s role in international health work—in research as well as other activities—occurs at a time when the Organization is assured of the support of practically all the countries of the world."

THE OBSTETRIC O.B.E.

Fashions for women change, even in obstetrics. Although castor oil had long been used to stimulate uterine action, its administration became more popular after B. P. Watson[3] had described, in 1920, a routine for induction which included a dose of castor oil. But, as we noted last year,[4] many obstetricians have now abandoned it as an unnecessary, uncomfortable, and inefficient infliction on the pregnant woman. However, Drs. J. G. Mathie and B. H. Dawson, in an article elsewhere in this issue (p. 1162), fight a gallant rearguard action for the cause of castor oil. They separated 75 women, all between the 38th and 41st weeks of normal pregnancy, into five equal groups. The first group received the full ritual of 2½ oz. (71 ml.) castor oil, followed by a soap enema and a hot bath (the "O.B.E."). The second group had only the castor oil, the third only the enema, the fourth only the hot bath, and the fifth had no treatment. From tocographic records taken before and after the respective treatments, the "index of contractile work done by the uterus per hour" was determined before and after treatment, and the percentage difference was calculated, the untreated group acting as a control.

Mathie and Dawson calculated that the full O.B.E. increased the contractile work done by the uterus by an average of 264%. The administration of castor oil alone effected an increase of 186%, of enema alone 95%, and of hot bath alone an insignificant 6%. They conclude that castor oil and a soap enema probably act synergistically to produce the full effect of the traditional O.B.E., the hot bath playing little or no part. They claim, therefore, that the marked increase in uterine action produced by the O.B.E. justifies its retention in obstetric practice as a method of inducing labour or as a prelude to other induction procedures. Unfortunately they do not state the actual results in their five groups in terms of the clinical onset of labour as opposed to the more academic calculation of the contractile work done by the uterus. Obstetricians will probably continue to recommend the use of the enema and the hot bath, if only for inner and outer cleanliness, but those who have given up prescribing castor oil—fortified as they are by the figures that only 5% of women at term and 20% after term start in labour within 24 hours of medical induction[5]—have greater confidence in other more certain if less innocuous methods of induction.

FOREIGN MEMBERS OF ROYAL SOCIETY

Two famous medical men were among the four new Foreign Members of the Royal Society elected last week. They were Professor G. Domagk, of Münster, West Germany, and Professor A. H. T. Theorell, of Stockholm. Both have been awarded the Nobel prize in physiology and medicine, Domagk in 1939 and Theorell in 1955. In a long career of fruitful research, Domagk's outstanding achievement was the discovery of the chemotherapeutic action of "prontosil," from which the sulphonamides were developed. He was elected a Foreign Corresponding Member of the B.M.A. in 1949. Theorell's work has been chiefly on the chemistry of haemoproteins and the enzyme mechanisms by which the blood transports and exchanges oxygen. It has been of great importance to the understanding of cell metabolism.

The report of the Scottish Committee on Prescribing Costs was published last week and is summarized in the *Supplement* (p. 202). The equivalent committee for England and Wales, the Hinchliffe Committee, is expected to issue its report soon.

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Drug Treatment of Disease

CORONARY ARTERY DISEASE: PART II

BY

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MYOCARDIAL INFARCTION

Early Treatment at Home

Since most patients with acute myocardial infarction require admission to hospital, the general practitioner is primarily concerned with the relief of pain, the immediate treatment of shock, the management of acute left ventricular failure, and the start of anticoagulant therapy. In most patients pain is relieved by the intramuscular or subcutaneous injection of morphine hydrochloride or morphine sulphate ¼ gr. or ½ gr. (15 or 30 mg.). When vomiting is known to follow the administration of morphine, a preparation containing the mixed alkaloids of opium (such as "omnopon") should be given intramuscularly or subcutaneously. The mild shock which often accompanies the onset of acute myocardial infarction usually responds to bed rest, warmth, and relief of pain. In contrast, persistent pain, sweating, and restlessness or a falling blood pressure indicate the need for immediate admission to hospital, since it may be necessary to combat cardiogenic shock with some of the measures outlined in the next section.

When the onset of myocardial infarction is accompanied by acute left ventricular failure ("cardiac asthma"), morphine ¼ gr. (16 mg.) should be administered intramuscularly as soon as possible; it can be repeated after an hour if necessary. Cardiac asthma is an occasion when the rapid administration of digitalis is indicated. Provided the patient has not been taking digitalis in adequate dosage during the preceding week, 1 mg. of digoxin, which is dispensed in alcohol, must be given intravenously diluted in 10 ml. of sterile water. If acute left ventricular failure develops in a patient already receiving digitalis and fails to respond to morphine, intravenous digoxin should be given only with caution and preferably by small doses of 0.25 mg., repeated after an hour if no intolerance develops. The slow intravenous administration of aminophylline 500 mg. over a period of 5 minutes is sometimes valuable in cardiac asthma, but the early administration of digoxin is the treatment of choice even if a myocardial infarct is suspected. Some relief from the acute distress of left ventricular failure is likely to be evident within 20 or 30 minutes of the intravenous administration of digoxin, but the patient should not be left unattended until asleep.

The value of the early administration of anticoagulants has now been established, and when there is no known contraindication (such as an active ulcer or liver disease) the practitioner should give a soluble heparin preparation, 20,000 units intramuscularly or 10,000 units intravenously and 10,000 units intramuscularly. If there is likely to be a delay of several hours before the patient can be admitted to hospital, an initial dose of one of the oral anticoagulants, which prolong prothrombin time, such as phenindione 200 mg. (four 50-mg. tablets) or ethyl biscoumacetate 1,200 mg. (four 300-mg. tablets) can be given when the first dose of heparin is injected. Subsequent doses of the oral anticoagulants must be adjusted according to the prothrombin time.

Early Treatment in Hospital

There are several complications of acute myocardial infarction which make it desirable for the patient to be admitted to hospital. These include shock, thromboembolic incidents, left ventricular failure, and paroxysmal ventricular tachycardia or other serious arrhythmias.

Cardiogenic Shock

The hypotension of cardiogenic shock often requires vigorous treatment. Severe shock is usually resistant to therapy, and it is important to start treatment as soon as possible. Although it is often difficult to decide when to start treatment, it is a mistake to wait until the patient is grey, collapsed, sweating, apprehensive, cold, and restless with a rapidly falling blood pressure. Nevertheless, many patients who appear shocked on arrival in hospital improve rapidly after lying quietly in a warm bed for an hour. The administration of oxygen at a rate of 6 l. per minute by a simple plastic mask or through a nasal catheter helps to combat the anoxaemia which accompanies cardiogenic shock.

As a broad guide, pressor drugs should be administered before the patient's blood pressure drops below 90/70. In a patient previously hypertensive, however, clinical signs of shock can develop at higher levels, and thus the blood pressure should not be the only guide. Pressor drugs, such as mephentermine sulphate 30 mg., which can be given by intramuscular or intravenous injection, are of limited value but can be administered at hourly intervals if necessary.

Noradrenaline is probably the drug of choice, though it has its disadvantages in cardiogenic shock. It must be given by intravenous infusion, 4–12 mg. in 400 ml. of isotonic saline. A suitable rate for infusion is 6–8 μg. per minute. Blood-pressure readings should be recorded at intervals of 15 to 30 minutes and the rate of flow adjusted accordingly. It is desirable to maintain the blood pressure at about 110/80, but it does not always respond to noradrenaline, and a pressor response is often difficult to maintain. Serious arrhythmias develop in 10% of patients. Although the treatment of shock is often disappointing, the early administration of noradrenaline may be a life-saving measure, particularly if reinforced by intravenous digoxin.

Since the administration of noradrenaline entails adding large amounts of fluid to a circulatory system whose efficiency is already impaired, the immediate risk of pulmonary oedema and congestive failure is considerable: it is all the greater if the heart has not been stimulated by digitalis. Cardiogenic shock of serious degree is invariably accompanied by signs of pulmonary congestion and by a greater or lesser degree

of cyanosis and dyspnoea. These features indicate the prompt use of digoxin 1.0 to 1.5 mg. intravenously and suitably diluted. Alternatively, ouabain 0.5 mg. can be given intravenously in an extreme emergency, and repeated once after an hour if necessary.

Thromboembolic Incidents

The risk of further thromboembolic incidents can be reduced by the administration of anticoagulants (Gilchrist and Tulloch, 1956). If anticoagulant therapy has not already been started, then on the patient's admission to hospital 10,000 units of heparin should be given both intravenously and intramuscularly, and 20,000 units of heparin injected intramuscularly 8 and 16 hours later. At the same time as the first dose of heparin, phenindione 200 mg. or ethyl biscoumacetate 1,200 mg. can be given orally. The dose of these anticoagulants (which are discussed in greater detail below) should be adjusted daily in order to maintain the prothrombin time between 2 and 2½ times the control value in seconds or the prothrombin activity between 10% and 20%.

Arrhythmias

It has already been emphasized that great benefit is obtained from the intravenous administration of digoxin in acute left ventricular failure. Similarly, digitalis is valuable in the *prevention* of left ventricular failure and is indicated if the patient develops orthopnoea or obvious basal crepitations during recovery from an acute myocardial infarct. Digitalis is also the drug of choice for the treatment of rapid auricular fibrillation and flutter following myocardial infarction. When auricular fibrillation accompanies acute myocardial infarction, it is sometimes paroxysmal and transient, normal rhythm returning within an hour or two without any specific treatment. If, however, the ventricular rate is rapid and greater than 120 per minute, or if the paroxysm of auricular fibrillation persists for more than 2 hours, digoxin should be administered intravenously. The heart rate must be obtained from auscultation of the apex beat, since the pulse deficit which is commonly present makes its assessment at the pulse unreliable. Uncontrolled auricular fibrillation or flutter soon leads to congestive failure. The drug treatment of congestive cardiac failure has been reviewed in an earlier article in this series (Campbell, 1958).

Paroxysmal ventricular tachycardia is not common, and its occurrence should be confirmed if possible by electrocardiograms before specific remedies are employed. Although quinidine is the drug of choice, ventricular tachycardia can sometimes be corrected by the intravenous administration of procaine amide: 1 g. of procaine amide should be diluted in 10 ml. of sterile water, and of this 1 ml. (100 mg.) can be injected each minute in the hope that normal rhythm will be promptly restored. More often paroxysmal ventricular tachycardia responds gradually to quinidine sulphate by progressive slowing in rate. Quinidine should be given in a dose of 3 gr. (0.2 g.) by mouth every 2 hours. If paroxysmal ventricular tachycardia persists after 36 hours of oral quinidine therapy, or if the patient is already developing signs of congestive failure, then the slow intravenous infusion of 3 g. of quinidine sulphate in 500 ml. of isotonic saline is indicated: a rough guide for this infusion is to give 50–100 ml. per hour. The heart rate must be carefully watched, and electrocardiographic control at hourly or two-hourly intervals is desirable. The drug must be stopped when normal rhythm has been restored or if toxic features develop. Quinidine sulphate 3 gr. (0.2 g.) or procaine amide 250 mg. should be administered by mouth four times daily for several days following the correction of ventricular tachycardia.

Long-term Anticoagulant Therapy

The patient who has recovered from a recent myocardial infarct may need drugs for the treatment of angina (see Part I last week) and for the prevention of further thrombotic incidents. There is increasing evidence that the administration of anticoagulants during the first year and possibly longer after infarction lowers the rate of recurrence of further infarcts, decreases their severity, and reduces the mortality (Bjerkelund, 1957). The choice of anticoagulant will have been made when the patient is in hospital. Two are commonly used in Great Britain, phenindione ("dindevan," "indema") and ethyl biscoumacetate ("tromexan").

Phenindione is more easily controlled, much less expensive, and is the long-term anticoagulant of choice. Its effect on prothrombin time, which is inversely proportional to the prothrombin content of the blood, is maximum in about 30 hours and has largely disappeared in about 60 hours after a single dose. This duration of activity and the lack of cumulative effect makes its administration easy to manage. It has few side-effects, but gastro-intestinal disturbances and dermatitis do occasionally occur; in these circumstances, ethyl biscoumacetate may be substituted. Tablets of phenindione contain 50 mg. and tablets of ethyl biscoumacetate contain 300 mg.; they should be given in divided doses twice daily according to the instructions issued by the hospital or laboratory responsible for the control of the patient's prothrombin time. Oral anticoagulants should never be given unless regular and reliable estimations of prothrombin time are readily available.

Anticoagulants act indirectly by decreasing prothrombin synthesis in the liver, and there are many available anticoagulants with varying speed and duration of action. Dicoumarol (50-mg. tablets), cyclocoumarol ("cumopyran," 25-mg. tablets), and phenylpropylhydroxycoumarin ("marcoumar," 3-mg. tablets) are three coumarin derivatives which have a delayed and more prolonged effect on prothrombin time than phenindione and ethyl biscoumacetate. This cumulative effect is a disadvantage, because their action cannot be counteracted as rapidly as that of phenindione or ethyl biscoumacetate. In particular, phenylpropylhydroxycoumarin prolongs prothrombin time maximally at 5 days and still has some effect after 10 or 12 days following a single dose. The administration of these longer-acting anticoagulants is difficult to manage, and they are not recommended.

The family doctor will find these differences in duration of action worth bearing in mind, because he may need to administer phytonadione (vitamin K_1) in the event of a haemorrhage. Haemorrhage is not common if the dose of anticoagulant is carefully controlled by prothrombin-time estimations, though unfortunately it does occur from time to time even when the prothrombin time is within the desired therapeutic range.

Haemorrhage occurs most commonly as minor subcutaneous bruising, minor haematuria, or minor

epistaxes and less frequently as large haematomata, haematemesis, or melaena. When phenindione or ethyl biscoumacetate are being taken, 25–50 mg. of vitamin K_1 orally is usually sufficient to restore prothrombin levels to normal within 18 to 24 hours. 10–20 mg. of vitamin K_1 given intravenously will have a quicker effect, but this is seldom necessary for a minor haemorrhage, since vitamin K_1 is active within three hours of its oral administration. Indeed, since anticoagulant therapy will be continued after the haemorrhage has stopped, only the omission of the anticoagulant for one or two days is usually all that is necessary for superficial bruising. It is undesirable to administer vitamin K_1 in the presence of minor bleedings, since the abrupt return of the prothrombin time to normal is sometimes associated with the development of further thrombosis. With the longer-acting coumarin derivatives, 50–100 mg. of vitamin K_1 orally or 25 mg. intravenously will be necessary in the event of a haemorrhage. If the family doctor finds it necessary to give vitamin K_1 or to reduce or stop the anticoagulant, he should refer the patient to the hospital or laboratory which is controlling the prothrombin time as soon as possible.

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THE TARDY CONVALESCENT

BY

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One of the most memorable French exercises I was ever made to perform—I must have been 9 or 10 at the time—was to translate into French a little anecdote which ran thus: "A lady called upon a doctor to examine a spot on her finger. 'It is a very good thing you lost no time,' he said. 'Why? Is it so very serious?' she asked. 'Had you waited until to-morrow, it would have disappeared,' he said, 'and I should have lost my fee.'" ("J'aurais perdu mon lolly," dit-il.)

I have always found this story very comforting; indeed, it may have unconsciously influenced my choice of profession: I don't know.

The fact is, luckily for most of us, that the animal body, the human psyche, and the divine spirit all strive to heal themselves when damaged, and to compensate themselves (in the non-litigious sense) when the damage is irreparable. This sometimes happens with our patients before we have got round to making a diagnosis. If we doctors ceased to exist, a working majority of our patients would get well of their own accord; and the human race would persist, not quite so uncomfortably overcrowded, perhaps, and not so geriatric-ridden; but it would get by. This may be the real reason why we never dare go on strike.

After the disease process has in the natural course of events burned itself out, after the physicians and surgeons have implemented such measures as stop the patient going downhill, by giving him something or taking something away, you might think that the patient would inevitably heal himself and regain a near-perfect state of health under his own steam? Not a bit of it. He will if he is an animal—a cat will streak across the lawn on three legs after a bird before the stitches are out of his amputation stump—but not if he is a human with the normal human fear of the unknown and human suggestibility. He usually enters a stage of convalescence; and how soon he will emerge from that stage into exuberant or subdued health depends upon several factors, of which the possession of sound wind and limb is, oddly enough, one of the least important.

Why is this? What are the forces that militate against return to full health?

Fear

First and foremost, obviously, is fear: fear born of ignorance or incomplete comprehension. Many patients, I find, embark on their convalescence without any clear idea of what has been happening to them; what has been done for them; the whys and wherefores; and what they may expect next. And with the vast majority of them, what they fear in their imaginings is much, much worse than the truth.

A middle-aged doctor surprised me at my first interview with him, before I had even outlined a tentative policy for his rehabilitation. He had had a small patch of bronchopneumonia with great constitutional upset. He had never had a day's illness in his life, and it had shattered him. He said, "I suppose I shall have to be pretty careful from now on? My wife has brought me long-sleeved vests and pants. Good thick ones, too. Like that stuff you stand typewriters on. They are going to take some getting used to. I'm used to wearing a thin singlet and shorts summer and winter alike." It was no use arguing with the man. It had to be deeds and not words. His rehabilitation took the practical form of nine-mile tramps around the country in all weathers, bicycling, sunbathing, and swimming. It took just over a fortnight, and he left in very good heart.

Women who have been parted from a nine-pound uterus which used to bleed furiously in and out of season don't realize that its removal enables them to enjoy better health and greater activity than they have experienced for years. They are often under the impression that the operation was performed merely to prevent them from getting worse; and they expect nothing better. The same applies to some who have had radical operations for prolapse or hernias. They have been mutilated and weakened, and must therefore be very, very careful in the future.

Where did they pick up these ideas? From the surgeons? It is most unlikely, except—and I shall return to this point later—where there is an ominous uncertainty implied by the request that they should attend the out-patient department in one, two, or three months' time. They feel they had better go slow until they have had this final "all clear."

They may have got the idea partly from hospital ward discipline, which lays such emphasis on bed rest, and allows no more exertion than sitting and strolling about the ward in dressing-gowns. It is possible that the last week or so of their hospital treatment is geared too low for their actual potentialities. Ward routine demands that after a certain point they seem to make no further progress.

And then, of course, they talk among themselves and compare notes. And they certainly have much to discuss. At Mundesley their discussions are unending and terribly inconclusive, for the patients are a random

collection from a number of different East Anglian hospitals who exhibit—I must not exaggerate—*not quite* 57 varieties of treatment for the same complaint. Billroth gastrectomy patients from one surgeon will be anxiously pingling a Witt III diet, while those from another surgeon are whacking into bottled beer and chops. One surgeon wants his herniorrhaphy cases to have three weeks of absolute bed rest, bed-pans and all; another will send them home on the third day with a memorandum to relinquish the stitches in a week, believing that, having removed a congenital sac, there can be no recurrence. Obviously the former patients will regard their cases as having been much more serious than those of the latter. *They* will have to be careful in the future and never lift a suitcase lest the wound bursts open and the hernia pops out again, and pops right out this time into their laps.

I mentioned bed-pans just now. May I digress? One of my great sorrows is that my late senior partner, Dr. Vere Pearson, never published his work on bed-pans. It was the fruit of really extensive research. Quite simply, he compared and contrasted bed-pans with bedside commodes as exercise-tolerance tests; and he found invariably that a patient's pulse rate and respiration rate were increased much more after using a bed-pan than they were after he had used a commode: thus confirming what all patients have repeatedly been telling us throughout the years: that it's a damned sight less exhausting to slide out of bed on to an adjacent commode than it is to balance and strain on an unfamiliar perch.

Complacency and Reluctance

Another reason, within the patient who makes a tardy convalescence, is *complacency*. Some patients, who are only too glad to be alive and freed from their pain, are undoubtedly inclined to rest on their oars. Especially is this true of the patient to whom his specialist has said, "Well, it was touch and go with you, old man; we nearly lost you." This gives him a special cachet, turns him almost into a museum piece to be admired and marvelled at, and a need to remain thus interesting as long as possible. This patient is quite the opposite of the one who boasts, "My surgeon said he'd never seen anyone who got on so quickly as I did." With her—and it's usually a she—I know I'm on a good wicket. She will press on like mad to retain her world title.

And then there is reluctance to be parted from the invalid's privileges. This I find is rarer than I had imagined; but when it is present there is no doubt about it. One of the reasons why I insist on seeing the patient's full case history before I see the patient is to get a bird's-eye view of his whole past health-sickness record and so know roughly what line of attack I should take at my first interview.

Recently I found myself addressing a professional invalid in these words: "Are you quite sure you really want to get perfectly well? Supposing I could wave a magic wand over you and make you fit, just think what it would mean. It would mean giving up bossing people around and making them fit in with your wishes. You'd have to find other things to talk about, other things to think about. *You might even find yourself having to do things for other people.* The sacrifices would be terrible. You've quite forgotten what it is like to be well. Are you sure you can make this sacrifice? I don't want your answer now. Think it over. Sleep on it. Take your time. I'm in no hurry. If you really want to get well, I think I can help you to help yourself. But you'll have to do all the work. There's no magic wand." And I wouldn't listen to any expostulations, but bade her sleep on it.

She didn't sleep very well that night. The next morning, when she told me she really did want to get well, I just shook my head in disbelief, and there I let the matter drop.

The days went by. She made a perfectly good convalescence. As she crossed the front hall carrying her suitcase to the waiting car and I went across to say good-bye, she turned on me in front of all the other patients loitering there—"You are a fine doctor, I must say, talking to me as you did when I first came here. I've never heard the like. I shan't come back here in a hurry." I bowed my head in shame. She got well to spite me.

I should mention one important extrinsic factor which may all too easily militate against convalescence and which I proudly claim as my own discovery.

A patient, when just ticking over 24 hours a day in bed in a hospital ward kept at a temperature of 70°, needs *fewer* calories than he does when he's up and about outdoors all day in a bracing sea climate and tramping five to six miles daily. At this stage he needs *more* calories; and *more still* if he is to regain the body weight he lost while in hospital. The effect of regaining this lost body weight on a patient's morale is incalculable. In a nutshell: inadequate food impedes convalescence.

An Early Experience

My first impact with convalescent homes was 30 years ago. In those days they were charitable institutions supported by voluntary contributions. Each one was associated with its own mother hospital, in whose gift its benefice lay—and a pretty rich gift it was too in those days for folk who could never afford to go away on holiday to be sent for a week or a fortnight to a seaside convalescent home. The honoraries and the ward sisters would confer and agree on which were the deserving cases.

My concept of the home itself, which I have cherished for these 30 years, and which may or may not be out of date by now, was that of a seaside establishment where these selected patients were sent as soon as they could make their own beds. It was presided over by a dear, chubby, soft-faced matron. The local doctors, who dropped in once or twice a week to sign certificates or take a look at problem cases, were so respectful towards her as to appear completely under her thumb, even if they didn't realize it.

After mooching about for the statutory 14 days, spent mostly in the common-room with the windows closed, smoking, playing billiards or cards, or listening to the wireless, the patient was sent home.

His G.P. now suddenly came back into the picture, completely clueless and unwillingly impressed by the patient that he must have been extra - seriously ill, because they had to send him away to the "Convalesunks" and he's only just back. So under the patient's guidance he prescribed a good strong tonic to build him up again, and issued still more club certificates pending some authoritative news and views.

Now this set-up obviously had its place, may still have its place. I am not decrying it; but even its most ardent supporters would allow that there might be room for improvement.

Presumably with something like this in mind, the East Anglian Regional Hospital Board decided by way of experiment to try opening a rather more high-powered convalescent hospital (or post-acute hospital as it is sometimes called) and rehabilitation unit; and I was put in charge, also experimentally.

Steps to Rehabilitation

Certain desiderata were mapped out, and more have emerged during the 21 months we have been functioning.

First, that rehabilitation should begin the very first day of arrival. If this is not to be mere lip-service to a good idea it involves an initial interview with the patient alone: alone, with no one else within earshot. A strange fellow-patient in an adjacent bed may embarrass and inhibit the newcomer; and if there is a sister in attendance I find I talk too loudly and start showing off. The interview has to be leisurely and of indeterminate length. It involves discussion, explanation, investigation into the patient's home set-up in some detail, and an assessment, usually only an impression, of the zest with which the patient faces the future—or his lack of zest.

Second, that rehabilitation should be progressive. Each day should bring "a step forward" whenever possible: hours up, exercise taken, and so on. This involves incessant exhortations, encouragement, praise and admiration, and a bit of mild bullying. Many elderly people, who for years have never ventured further than round the corner to the shops or to the nearest bus-stop, are amazed to find themselves, in less than a fortnight, rejuvenated, tramping the three hilly miles to the seashore and back with zest.

Third, that the patient should not only become fit but that he should become confident that he is fit. This is not always possible. Should his illness have left him with a partial incapacity, he needs to discover the extent of this residual disability and learn to live, and to live confidently, within his new limitations. This makes the job really worth while and enviable, for it means quality rather than quantity. Each patient has to be studied individually. With some, the end-point is reached when they "haven't felt so well for years," and are ready to plunge back into their normal employment without any qualms—and without further weeks on sick benefit. With others it may mean only going home, living on the ground floor, and having the minimum amount of home help.

Oddly enough, this criterion does not interfere with turnover as much as I had expected: for the average length of stay is only 22.7 days. It is also the hardest criterion to fulfil. The patient who has had a couple of coronaries while in hospital doesn't feel completely foolproof, even after he has demonstrated to himself that he can climb stairs and walk three hilly miles to the seashore and back. Girls under their mother's domination—and I've had as many as four of these at one time—have not got the same inner drive to get back into harness as girls on the brink of matrimony have. Sometimes something can be done by almoners, welfare officers, and such to alleviate the conditions which face the patient at his discharge. Sometimes the patient can come round to a more tolerant, more creative, attitude towards his difficulties. More often than not, a lot of work and thought can be expended in this field without showing any results at all; but the results, when they do come, are richly rewarding.

Fourthly, that the G.P. should be put into the picture no later than the same day the patient gets home. This is really very easy. Notes have got to be made up and letters written some time, so why not on the day before the patient leaves instead of several days later?

Specialist Follow-up

Comes the day when I make up the final notes and draft the report to the G.P.; and I look at the original application form. Does the hospital consultant want to see the patient in his out-patient department? In 19 cases out of 20 the answer is yes, he does. "To come up in a month's time."

In at least three cases out of ten that pass through my hands a specialist follow-up is entirely unnecessary.

Obviously in cases of malignant disease and cases of chronic progressive disease results and progress should be checked and followed through by experts with all their armamentarium of *x*-ray films, cardiographs, pathological investigations, and expert knowledge. Consultants naturally wish to follow up cases of unusual interest, and they should be allowed to do so, if the patient's family doctor feels it is not likely to prove detrimental to the patient concerned. It must be rather nice, too, for them occasionally to see an ex-patient whom they have successfully helped to regain his health, amid their schools of recurrent chronics. One should not deprive them of all their fun. But so very often it is their registrars who see the old cases. In at least three out of ten cases which have undergone routine surgical operations or run-of-the-mill medical episodes, the specialist follow-up is an unnecessary ritual. It is also harmful.

The patient concerned is not allowed to put his illness or his operation into the past where it belongs. He is not allowed to cease being a patient. Looming ahead of him lies that visit to the hospital; presumably, he thinks, to make quite, quite sure that all is well. So there must be some doubt about it even now. So he is subjected to further anxiety and suspense. It also hamstrings the patient's G.P., who dares not make any radical changes in the patient's regime while he is still under hospital treatment. The G.P. is no longer in control. He dare not even allow the patient to go back to work, lest it seem premature. Should he do so, when the out-patient appointment falls due, the patient will have to lose a day's work, and fight against terrific odds to get free transport laid on for him.

Role of Nurses and Orderlies

No account of rehabilitation would be complete without reference to the part played by nurses and orderlies.

Nurses receive their training in the wards of general hospitals, where the patient is very much the under-dog. On admission he is divested of his clothes, so he cannot walk out in a huff, as you and I would walk out of a hotel where we did not get the service we expected. At the outset, too, he is broken in by being kept in bed. This does not merely strip him of his manhood: it reduces him to infancy and an infantile dependence upon the mothering nursing staff. The association of ideas between "being a bad boy" and "being kept in bed" seems ineradicable. A bed-patient will say of a relapse, "I've been misbehaving myself again, doctor":

a remark which no patient clothed and in his right mind has ever been known to utter.

The ward set-up is matriarchal. For 24 hours of the day he is at the tender mercy—and I am not denying that it is a tender mercy—of the nursing staff. Every day, Daddy, in the shape of consultant, registrar, houseman, or whatnot, drops in for a comparatively short time, not much more than 10% of the total hours; and he seems concerned mostly with temperature and urine output charts, *x*-ray films, and pathological reports—the good behaviour, medically speaking. With matters of ward routine he rarely interferes: in these matters "Mummy knows best."

There is a school of thought that discerns a hierarchy, a Pecking Order, within the matriarchal group. It maintains that the fledgling nurse in a hospital ward is a bit scared of everyone, including even the patients; but with the patients—obviously the lowest form of life—she feels she has something in common, and she may actually take their side at first. But she soon grows out of this, and when she demonstrates complete ascendancy over all patients she is given her colours; ascendancy over housemen and registrars and she's a staff nurse; over visiting consultants a sister; ascendancy over the whole boiling lot, including house committees and hospital management committees, and she's a matron.

Now, I'm not quarrelling with this set-up. It has stood the test of time. Although not necessarily perfect, there is nothing to beat it as a haven for the sick and weary. I would even go a long way with the Freudians, who claim that illness necessitates regression to childlike reactions and behaviour, and needs loving care from mother and father figures. And I would go further. The return to full health involves a growing-up, a weaning from the mother, and, eventually, a rebellion against paternal domination.

To revert: until the day of his discharge the patient in a general ward usually remains deprived of his clothes, and leads at most a slipshod existence in pyjamas and dressing-gown. Bed is obviously the right place for him: to be allowed out of bed is a privilege. He has to hop back into it again for the doctor's rounds, and for visiting hours. In between whiles the more ambulant patients may be given little errands and other servile jobs to do, and so earn some good marks. How eagerly and officiously do they comply.

Not only is the patient assumed to be helpless, he is also assumed to be dim-witted and irresponsible. Maybe quite rightly; he may have been helped to regress so successfully that, no matter how mature, responsible, and integrated he used to be in everyday life, under ward conditions he has travelled backwards to the mental age of 3 minus. He cannot be trusted to take his own temperature or his own medicines. At appointed hours a nursling trots round and spoonfeeds him. His lifelong experience concerning which aperient or hypnotic or what diet suits him best is ignored; and he does not endear himself if he proves that, as he foretold, the routine stuff fails in its purpose. In next to no time the word goes round that he is a difficult patient, subversive, a trouble-maker, and a bad influence on the ward morale, to be treated with hauteur and to be got rid of as soon as possible.

I know what I'm talking about because it has happened to me, a most inoffensive chap. I merely pointed out—— But I won't go into all that.

The ideal patient is one who conforms utterly, submits to absolute regimentation, and, of course, exudes appreciation at every pore.

I have painted this picture in good strong colours because I want to make the point that when nurses, who have trained and worked quite happily in that night-nursery climate—when they undertake convalescent nursing, they often don't like it at first. In fact, they may never come to like it, for it needs considerable reorientation.

As I have said elsewhere, it is most noticeable that nurses prefer their patients to be helpless, and the more helpless the better. Why? A heavy case means hard work, and hard work is always satisfactory; but in addition the helpless patient, however crotchety, is emotionally rewarding, giving the nurse the heart-warming feeling that she is *needed*. To lose this status of being needed can be almost as upsetting as being jilted.

Nurses are not alone in displaying this reaction. After all, the patient is merely a neighbour to whom we are able to offer timely help. We are all apt to forget this, and to regard him as a personal possession, a loyal private in our little army. Should he desert to another leader, we feel smaller in stature, and mourn, not our financial loss but our loss of prestige. We tend to cling most to those patients who are emotionally rewarding, and to prolong their dependence upon us. Conversely, some of our patients seem to postpone their complete recovery almost indefinitely in order to maintain their bond of union with us. That is by the way, but it helps to emphasize the tremendous part that interpersonal relationships, operating unseen, play for good or bad in the healing art.

To return: We are all very much better at helping a patient than at helping the patient to help himself. It is easy and quite instinctive to support—almost to carry—the tottery bedridden patient on his first walks; but the subsequent stages of "one hand" control, and then "one finger" control, and the stage of "being there ready," accompanying but not in actual contact with the patient, are nothing like so alluring. Why? I suppose because "doing" is rated more highly than "being": it is more showy.

It is traditional for the patient while in hospital to have his medicines administered dose by dose at the appointed hour—like a child. When he is destined to take his digitalis pills for a considerable time after he gets home, you might think that he should be helped to grow up, and be trained to help himself, unprompted at the right hours, from a private personal store, to be replenished every week. Should he then slip up with either an overdosage or an underdosage he is still in the right milieu for this accident to be dealt with.

If the patient is a slightly ga-ga grannie who is going to be looked after by an ever-loving unmarried daughter this training is unnecessary. Each case should be decided upon its merits; but self-help should be the rule and not the exception.

So you would think. But with what hostility does this unorthodoxy meet whenever I suggest it. Oddly enough, patients can be taught to manage their own colostomy toilets, the diabetics to measure out and inject their own insulin, and the asthmatic is allowed to keep his atomizer at hand and sometimes even his own emergency "franol" tablets and aminophylline suppositories. But there the line is drawn. Patients to

(Continued at foot of next page)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Lapudrine (Imperial Chemical Industries).—This is chlorproguanil, a new antimalarial having pharmacological properties similar to those of proguanil but with the important difference that it is more persistent in the body. It may thus be administered in a weekly dosage instead of daily, as is required for prophylaxis with proguanil. It is effective against asexual erythrocytic forms of all malaria parasites, but is especially active against primary exo-erythrocytic forms of *Plasmodium falciparum*, against which parasite, therefore, it acts as a causal prophylactic. Tablets of 20 mg. are available.

The recommended dosage is 20 mg. weekly, the initial dose being taken on entering the malarial area and at least one dose being taken after leaving it. The drug is well tolerated even in amounts considerably in excess of that recommended, and side-effects are unlikely to occur. A very carefully conducted series of trials had been held on this drug, and it promises to be a useful and cheap addition to the existing range of malarial prophylactics.

N.H.S. basic price: 200 tabs. 16s. 3d.

(*Continued from preceding page*)

take their own medicines two or three times a day or at night? Good gracious me, no. The objections range from, "Supposing they forget, or take an overdose, who would be responsible?" to, "You will lose all your nurses if you take away all [*sic*] their duties and responsibilities." I am intimidated by bogies and blackmail, on top of conservatism.

Conclusion

The rehabilitation of convalescents is like the wise upbringing of children: it entails a change in relationship. The baby in its cot must grow up to full adulthood and reach equality with his parents, real or surrogate. Domination and ascendancy must be relinquished with good grace. During the growing-up period it also entails being alert and ready in case of a fall, and suffering agonies in silence when they start climbing trees and riding bicycles in the High Street. But play for safety, hedge around with apron-string restrictions, check initiative, curb experiment, and you inhibit the child's growth and development. It needs courage and fortitude to take the inevitable risks.

Risks have to be taken which never arise under hospital ward regimentation. How can one know when a cardiac case can safely cope with his stairs at home until one has tried him out walking up a flight in the hospital? A moment comes when the risk is adjudged slight enough to be justifiable. The peptic ulcer patient must learn by trial and error how far he can stray from his GIII diet. The housewife, blithely put on a salt-free diet, is eventually going to find the dual cooking involved too much for her, and inevitably will abandon it sooner or later. Should she not try abandoning it while under medical supervision to see whether in her particular case it is really necessary?

The occasional setback, the occasional error of judgment, are inevitable, but when explained and discussed frankly they add to the patient's self-knowledge. They are worth it: for the alternative to taking risks is to eject patients back into their world uncertain, fearful, half-cock, and very often a burden to others; and what is worse—still patients.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Top Surgeons

SIR,—I am reassured to find that you share my feeling of distaste for the methods being employed in the present publicity campaign of the English Royal College of Surgeons (*Journal*, April 25, p. 1100). I was wondering if I was being a bit priggish. Apart from its shameless vulgarity, on which you have commented, the exaggerations and false implications of the campaign give the impression that the College has allowed the advertising company handling its "account" to apply too freely the lessons of its previous experience in the promotion of detergents. I wonder what the Edinburgh College thinks about it?

Is it true, for instance, that the College of Surgeons of England bears the main responsibility for education in surgery? I thought that it was an examining rather than a teaching body, and that for over a hundred years the main responsibility for all aspects of medical education had lain with the medical schools. Can Sir Alexander Fleming and penicillin be claimed as products of the College? I had heard—but perhaps the story is untrue—that the officers of the College themselves did not realize that Fleming had years before obtained the fellowship of the College by examination until they offered him an honorary fellowship after he had achieved fame by the discovery of antibiotics. Is it justifiable to imply that the College has been a major contributor to the development of such medical sciences as biochemistry and pharmacology? I had the impression that in as far as members of the medical profession had contributed to the development of such sciences they had usually been physicians rather than surgeons.

This sort of publicity technique both in overt advertisements and in "editorial publicity" has led the consumer to develop a cynical and sceptical attitude to much of what the advertisers say. It will probably have the same effect upon the public's attitude to one branch of the medical profession, for it gives the impression that the officers of the College are prepared to do or say almost anything to get money for it.—I am, etc.,

Leeds. G. R. HARGREAVES.

Food-poisoning and Food Hygiene

SIR,—In your leading article (*Journal*, April 18, p. 1023) you mention the need for an expansion of education in the important field of food hygiene. You rightly point to the value of courses of instruction for public health inspectors and for those concerned in the preparation of meals. Yet it seems to me that one valuable means of propaganda remains unused.

Every housewife and, I suppose, many institutional cooks use cookery or recipe books. In my own household we have half a dozen of these (including one published by the British Medical Association), but in none is there any advice on the prevention of food-poisoning. A short but authoritative chapter in the popular cookery books, such as those issued by makers of gas and electric cookers, explaining the nature of food-poisoning, its manner of spread, and the methods of preventing it would reach many more cooks than

those attending courses of lectures. The B.M.A. should certainly set an example by including such a chapter in the *Family Doctor* recipe book.—I am, etc.,

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Respiratory Difficulties at Birth

SIR,—Dr. R. J. K. Brown's commendable review "Respiratory Difficulties at Birth" (*Journal*, February 14, p. 404) is symptomatic of paediatricians' growing concern with basic science, and we too have become intrigued by the dramatic adjustments from the foetal to the neonatal state. However, Abrahamson's rhetorical "What have we done in resuscitation of the newborn infant with respiratory distress?" is a somewhat inept opening to a discussion which has little bearing on this very important subject.

The statement that "numerous drugs, methods, and machines, recommended for resuscitation, testify to our ignorance" is only partly true. As long ago as 1933, Wilson and Farber[1] showed that a pressure of 35 cm. of water was necessary to inflate the excised newborn lung, and that the re-expansion of collapsed lungs demanded even higher pressures. Day and his co-workers,[2] also using human stillborn and neonatal lungs, showed that the safety of high pressures depended on brief times of exposure and recommended 40 cm. of water at 0.15 second bursts as safe and efficacious for the initial expansion of both primary and secondary atelectatic lungs. An elaboration of this work, based on the different form of the pressure curve in deflation, suggests that the maintenance of 5 cm. of water positive pressure in the expiratory phase reduces surface tension forces by encouraging a residual alveolar volume, and thereby facilitates inflation.[3] Thus, there is now little doubt as to the basic requirements of the ideal mechanical resuscitator, and the multiplicity of machines is more attributable to a lack of ingenuity than ignorance. What is needed is a compact apparatus which can deliver, at known rates between 30 and 40 per minute, known pressures up to 40 cm. of water at known bursts up to 0.5 second with a known interval pressure of 5 cm. of water, and, after expansion has occurred, lower pressures automatically or synchronous with the infant's own respiratory efforts. The nearest approach to these principles has been used to good effect by Donald *et al.*[4]

With regard to the ideal concentration of oxygen, 100% is known to predispose to pulmonary irritation, atelectasis, haemorrhage, and retrolental fibroplasia, and concentrations of 30% or 40% are probably adequate. Dr. Brown's statement that "the establishment and maintenance of the 'correct circulatory pathways' after birth is essential for . . . survival" is highly dangerous if it persuades anyone to attempt to influence the "circulatory pathways" while neglecting the proper use of oxygen. Although the haemodynamic changes of the newborn are academically exciting, it is as well not to forget that most infants with congenital malformations of the heart and vessels survive the first three days without difficulty. In our view, the all-important principle in the resuscitation of the apnoeic or dyspnoeic infant is to make adequately oxygenated blood available to the body, and this can hardly be over-emphasized. As yet, the infant's own lung is still the best available oxygenator, and, likewise, the availability and direct control of mouth-to-airway resuscitation is hard to equal.[5]

Referring to the work on venous pressures by Bonham Carter *et al.*,[6] Dr. Brown's suggestion that the readings might have reflected portal vein pressures is incorrect, since the catheter was ". . . passed up the umbilical vein for 5 to 8.5 cm. *until the meniscus rose and fell freely with respiration.*" His objection to the considerable evidence in favour of placental transfusion (e.g., Gunther[7]) is the more surprising in view of the enormous umbilical vein pressures which can be recorded in the third stage of labour when uterine contractions on a vascular placenta elevate these pressures to 100 mm. of mercury.[8]

The pulmonary hyaline membrane is probably the most important single problem in paediatrics to-day, and Dr. Brown has rightly devoted much space to it, but here too we would take issue with him. It is certainly not our view that "delayed onset of respiration is a most important factor in its aetiology." When defined as the onset of regular respiration more than 5 minutes after delivery, some 10% of all our live-born infants show a delayed onset of respiration. Yet the pulmonary syndrome is seen only in the prematures and delayed onset of respiration is not a particular association. That aspiration of amniotic fluid plays no part whatsoever has never been claimed by Gitlin and Craig,[9] who, on the contrary, suggested that amniotic thromboplastin assisted in the conversion of fibrinogen to fibrin in the alveolar exudate. Interestingly enough, the causes for delayed onset of respiration listed by Dr. Brown (e.g., foetal distress, intrapartum asphyxia) are precisely those known to induce foetal respiratory movements with consequent inhalation of the amniotic contents.

Dr. Brown clearly favours the hypothesis that asphyxia and alterations in systemic/pulmonary pressures cause pulmonary hyaline membrane disease. It is true that James and Rowe[10] showed that hypoxia in the normal newborn caused a fall in the mean systemic arterial pressure (average 21%) and a rise in the mean pulmonary artery pressure (average 17%). However, these changes required first an average fall in arterial oxygen saturation of as much as 55% and, in any case, led to a reversion to the foetal pattern of circulation with a diminished pulmonary blood flow. Moreover, cardiac catheterization studies in infants with hyaline membrane disease have demonstrated not only virtually normal systemic and pulmonary pressures but also normal arterial oxygen saturation, except terminally.[11] There is certainly no evidence that these infants suffer from prolonged asphyxia in the initial stages or that anoxia ever leads to hyaline membrane disease experimentally.

Any discussion of hyaline membrane disease is incomplete without reference to the major contributions of Karlberg *et al.*[12] to our understanding of the basic pulmonary dysfunction in this condition. They showed that, whereas normal infants exert a negative pressure of 5 cm. of water in quiet inspiration, the infant with respiratory distress uses negative pressures of 20 to 30 cm. of water to effect the same tidal ventilation. In other words, these infants' lungs are either too inelastic or the alveolar walls "too sticky"; they must work harder to breathe, and, terminally, their respiratory muscles become exhausted. What we must ask ourselves is whether such enormous pressure swings, continued some 40 to 50 times per minute for many hours, are in themselves capable of damaging the pulmonary capillaries of the premature infant. And could this abnormally high negative intrathoracic pressure itself in some way be responsible for the left to right shunt through a potentially open ductus arteriosus?

Observations on animals, which Dr. Brown quoted extensively, have shed much light on human problems, but it would be a mistake to carry the analogy too far. We heartily endorse his stricture that "respiratory and circulatory functions cannot be separated." We

must now pay more attention to the pulmonary physiology of the *human* neonate.—We are, etc.,

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Quinidine and Muscle Weakness

SIR,—Reversible muscle weakness after quinidine, as reported by Dr. P. L. Colville (*Journal*, January 31, p. 281) in a child that suffered from attacks of paroxysmal tachycardia, corresponds to effects of quinidine which can be produced in the experimental animal. In a cat weighing 2 kg., 30 mg. injected into a femoral artery caused a slight and slow decline of the response of the ipsilateral gastrocnemius to direct stimulation, while neuromuscular transmission was depressed for ten minutes only when tested by stimulation through the motor nerve. The twitches in the other leg were not affected although the amount of quinidine which reached the general circulation was sufficient to lower the blood pressure level. Only after much larger doses or after repeated injections of the alkaloid occurred marked depression of the response to direct stimulation and complete neuromuscular block which lasted for several hours.

The Wolff–Parkinson–White syndrome shown by the case under review is in young people not usually connected with apparent heart disease.[1] In Dr. Colville's patient, however, diffuse cardiac enlargement was present. If this finding was associated with defects of the peripheral circulation—e.g., deficient oxygenation—such an impediment might sensitize skeletal muscle to the depressive effect of quinidine.—I am, etc.,

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Carpal Tunnel Syndrome

SIR,—I have recently seen six cases of carpal tunnel syndrome. The last two occurred in pregnant women, giving symptoms within the first three months of pregnancy. It struck me that in these cases in pregnancy the cause may be due to salt and fluid retention. Treatment with chlorothiazide, a maximum of two pints of fluid daily, and no added salt at the table, has in both cases abolished all the symptoms of aching and paraesthesia. I have discussed these cases with an orthopaedic surgeon who has operated on over 300 cases of carpal tunnel syndrome, and he believes the cases in pregnancy are due to salt and water retention.

One can also abolish the symptoms with the above regime in some cases which are not associated with pregnancy, but it would appear sensible to operate on these early on.—I am, etc.,

P. J. GULY.
Bushey Heath, Herts.

Telling the Cancer Patient

SIR,—If Professor H. C. McLaren (*Journal*, April 18, p. 1039) is certain that his patient with carcinoma of the ovary does not suspect the true diagnosis he may be justified in trying to deceive her. The trouble is that the present "hush-hush" and conspiracy of silence concerning cancer has brought about a position in which more and more people utterly distrust their doctor if there is any suspicion of cancer in the case. I know this to be a fact because they write to me, and I have to make excuses for the medical profession. Cases of true cancerphobia, of which fortunately there are only a few (each year one or two commit suicide), are often caused by the attitude of the medical profession. Admittedly in some cases it is difficult to decide whether to tell a particular patient, but the present principle of always telling the relatives everything but the patient nothing is in my opinion quite wrong for the following reasons:

(1) It is very doubtful if a patient who is becoming more and more ill can continue to be deceived. He or she may pretend to be in order to please relatives or the doctor.

(2) When the patient does realize the truth he believes that the doctor is at fault because he did not diagnose it earlier when he first became ill.

(3) When a patient, a relative of the deceased, in later years thinks he has cancer the doctor will find it difficult to convince him otherwise, as he knows the late relative was deceived by his doctor.

(4) I am convinced that most patients prefer to know the truth, however unpleasant, rather than be left with uncertainty. The Manchester figures (*Journal*, March 21, p. 779) suggest this very strongly.

(5) If the public never hear of a case that has been "cured" (and they never will from Professor McLaren), naturally they will not go to a doctor if they think their condition may be due to a malignant disease.

(6) Most patients who know they have been operated on for cancer believe that they have been "cured," *a belief which must be kept up to the very end.*

Many doctors funk telling a patient, and Bonney's "great blessing" is for the doctor not the patient. Once cancer education has succeeded in "making cancer ordinary" (see the Manchester report) half these problems will disappear.—I am, etc.,

MALCOLM DONALDSON,
Honorary Secretary,
Cancer Information Association.
Oxford.

SIR,—Surely the answer is always to answer truthfully all questions of patients. If they do not want to know, they are unlikely to ask; if they do ask, they have the right to a truthful answer. If a doctor does not always tell the truth, no one may know which is the lie.—I am, etc.,

G. C. MILNER.
Wittersham, Kent.

Spinal Analgesia in Obstetrics

SIR,—Mr. R. T. Sears's account (*Journal*, March 21, p. 755) of his experiences with spinal analgesia raises certain points which it would seem necessary to emphasize.

Until the beginning of World War II, the obstetrician was in many instances dependent for anaesthesia in any operative procedure either upon the services of what

would now be described as the "casual" anaesthetist, or upon the use of spinal analgesia, very often administered by himself. Indifferent experience led, partly in desperation, to the widespread use of local analgesia in some centres, though during the war years, for other reasons, spinal analgesia was, I think, widely used. Since the end of the war the picture has completely changed in many places. The skilled anaesthetist has taken an ever-increasing interest in anaesthesia for obstetrics. Of course we are all well aware of recent papers stressing the dangers of inhalation vomiting, as if we were hitherto unaware that obstetrics in all its aspects is very often a dangerous pursuit. Latterly it is just this very danger over which the modern, skilled anaesthetist has given us so much help.

Under present circumstances, when co-operation between obstetrician and anaesthetist has reached a most satisfactory level, and should be increasing still further, it seems to me unfortunate that the continued use of spinal analgesia should be advocated. Mr. Sears is fully entitled to use it, and the courts, as yet, will support him if disaster follows, provided he has shown all reasonable skill. But he is not entitled to expect me to forget the mishaps of a generation ago, though admittedly they almost all occurred in cases of caesarean section, nor can I deliberately ignore the advice of my anaesthetist colleagues for whose opinions and practice I have come to hold great respect, and upon whose help I am almost daily reliant.—I am, etc.,

Liverpool, 1. H. VINCENT CORBETT.

SIR,—We have read, both with interest and astonishment, the article on the use of spinal analgesia in forceps and breech deliveries (*Journal*, March 21, p. 755) by Mr. R. T. Sears. This article is, to our minds, self-condemnatory by its very praise of spinal analgesia, because the complications of the technique are so frankly listed. To mention some: hypotension, spinal shock, meningitis, ocular palsy, and headaches. Mr. Sears says that mothers interviewed after delivery "seem well satisfied with their experience." This surely does not agree with the statement that 14.1% complained of headaches for from three days to three weeks.

However, we would stress that epidural analgesia, by a caudal or a lumbar approach, has great advantages over the "spinal" method, providing a "saddleback" anaesthetic without the risks—and serious risks—attributable to a "spinal block." Moreover, in cases of prolonged labour due to cervical dystocia, caudal epidural anaesthesia has undoubted merits. With such experience, of course, this technique need not be of an "occasional nature."—We are, etc.,

M. B. WINGATE.
HAROLD C. J. BALL.

Southampton General Hospital, Southampton.

Anaesthesia in Domiciliary Midwifery

SIR,—Dr. Bryan Williams (*Journal*, April 4, p. 922) mentions the risk of giving open ether in a room with a fire. He suggests rather drastic treatment for the fire. The risk of ether catching fire may be minimized by putting a clothes-horse in front of the fire, draped with a large sheet, of which several inches should be on the ground. If the sheet is then soaked with water, particularly at the bottom, the risk of ether catching fire is reduced to negligible proportions.

In pre-war days I have many times used this method when administering anaesthetics in domiciliary midwifery.—I am, etc.,

Department of Anaesthesia, Charing Cross Hospital Medical School, London, W.C.2. H. K. ASHWORTH.

Vulval Varicosities in Pregnancy

SIR,—I see from the *Journal* of March 28 (p. 831) that Mr. Harold Dodd and Dr. H. Payling Wright recommend an extensive operative procedure for varices of the vulva, which they are prepared to recommend until "up to the end of the seventh month." I would have thought that a simple induction of labour shortly after that time would have been a far more sensible procedure, since the varices would then subside to such an extent that either they would require no operation or surgery would at any rate be made simple.—I am, etc.,

London, W.1. R. ROWDEN FOOTE.

SIR,—Mr. H. Dodd's and Dr. H. Payling Wright's article on vulval varicose veins during pregnancy (*Journal*, March 28, p. 831) very rightly calls attention to a fairly common complaint of pregnancy which is only slightly dealt with in textbooks.

Apart from very occasional superficial thrombosis during delivery, I have never seen any serious complication of this condition. On the other hand the authors are quite right in describing the condition as "distressing": it is very painful and incapacitating. I find it so in much more than 2% of my patients, obviously because in my G.P. practice I see a far greater proportion of multiparous women compared with the authors' hospital experience. The turgidity of the labia on standing produces pain and a burning sensation. A pain is also felt often in the sacral region. The condition predisposes to intertrigo and incapacitates the pregnant woman to a varying degree.

There are two features of the condition which I would like to add to the description by Mr. Dodds and Dr. Payling Wright. (1) Once a congenital weakness of the venous plexuses has been precipitated into varicosities of the vulva by pregnancy, the trouble perpetuates itself for the child-bearing period, and causes distress during every pre- and intra-menstrual period. (2) The condition is not recognizable on the examination couch, unless it is of an extreme degree. The patient has to be examined standing up, and that should be done when the woman is a young and healthy expectant mother, and complains of undue fatigue, as the sense of heaviness, comparable to the pain and heaviness of varicocele, leads to a feeling of perpetual tiredness. The gradual onset during gestation makes it sometimes difficult to elicit as a pointing symptom.

The comparison with varicocele led me to attempts at treatment of the condition by support. As soon as I recognized the presence of vulval varicosities I advised my mothers to wear "elastic pants." These are very easily obtained at any outfitters. The pants should be "all-round-stretchable," and not too deep, so as not to constrict the abdomen. The garment is washable and can be got for as small a cost as 25s. I have found this treatment on the whole successful, and on the strength of that I wrote in 1955 to the Ministry of Health asking for "elastic pants" to be added to the schedule of appliances prescribable by general practitioners. The answer was in the negative, as discretion was considered safer in the hands of hospital consultants. On reflection perhaps it saved the Service some money; anyway, if I find mothers too poor to buy the pants, I prescribe crêpe bandages and instruct them to make a T-shaped support. Some relief can be obtained from this.

No doubt there are a number of cases for whom the operations described in the article and performed after confinement, when the vulval varicosities refuse to improve, will mean all the difference between severe handicap and the feeling of wellbeing and strength. The surgical procedures described, undertaken during pregnancy in a very highly vascularized field around the pregnant uterus, would need a very strong and urgent indication indeed.—I am, etc.,

Bexleyheath, Kent. A. KOBY.

Smoke Vapours and Carcinogenesis

SIR,—In studies of factors that might give rise to lung cancer, emphasis seems to have been placed hitherto on the particles present in polluted air and in tobacco smoke. This may be due in part to the fact that some aerosol particles are known to cause certain diseases of the lung.

In particular, some evidence suggests that aerosol particles cause cancer of the lung in workers in the chromate, asbestos, and metal industries.[1] Furthermore, there appears to be an increase in the incidence of lung cancer with increase in the mass concentration of particulate atmospheric pollution.[2] Carcinogenic compounds have been found in the particle phase of general atmospheric pollution,[3 4 5] and some of these particulate samples have been used to induce skin cancer in mice.[6] Similar results were obtained with the particulate phase of automobile exhaust fumes.[6] Carcinogenic compounds have also been found in tobacco smoke condensates collected at about −80° C.,[7] and skin cancer has been induced in laboratory animals by the application of tobacco smoke tars.[1]

Although Neve,[8] Waller,[3] Davies,[9] and Weller[1] have mentioned the possibility of some contribution by the vapours of smokes to carcinogenesis, discussions of the factors involved usually emphasize the importance of the particle phase.[2 3] However, there is some reason to doubt whether the particle phase of certain smokes is of overriding importance. In discussing the possible effects of tobacco smoke Davies[9] pointed out that, although lung cancer appears to develop first in the bronchi rather than in the alveoli, it is to be expected on theoretical grounds that tobacco smoke particles, which are about 0.1 μ radius, are probably deposited less copiously in the bronchi than in the alveoli. Furthermore, it is likely that the percentage retention of particles in the human lung as a whole is minimal, or nearly so, for particles whose radius is about 0.1 μ.[9 10] There appears to have been no systematic study of the relative rates of deposition of the vapours and the tarry particles of tobacco smoke in the human lung. The results of recent studies of physical properties of wood smoke[11] might therefore be relevant.

Wood smoke was generated under conditions similar to those obtaining during the generation of tobacco smoke. It was shown[11] that, as is the case for tobacco smoke, freshly generated wood smoke contains vapours and gases and tarry droplets of the order 0.1 μ radius. Measurements were made of the rates of deposition of wood smoke on dry and wet surfaces when the smoke was passed over them. The rate of deposition of wood smoke on dry metal surfaces was determined by weighing. To estimate the quantity of smoke deposited on wet surfaces such as water, the "smoked" water was freeze-dried and the residue taken as an index of the quantity of smoke initially deposited. Some of the deposited matter must have evaporated during the process of freeze-drying, and the figures obtained were therefore possibly lower than the true rates of deposition. The residues resembled bulk samples of the particle phase of wood smoke, being tarry, dark in colour, and relatively non-volatile.

The rate of deposition of wood smoke on wet surfaces was found to be considerably greater than that on dry surfaces. The rate of deposition on water of smoke containing both particles and vapours was compared with the rate of deposition of the vapours alone, the particles having been removed by means of an electrical precipitator. It was found that the rates of deposition with and without the particles were the same, when the other physical conditions of smoking were equal. Similar results were found for smoke generated in a fluidized bed of wood sawdust using heated air at a constant temperature. This was the case despite the fact that the mass concentration of the vapour phase of this wood smoke (condensed at about −80° C.) appeared to be much less than that of the particle phase. It may be concluded, therefore, that the tarry residues obtained by freeze-drying smoked water resulted mainly from the deposition of wood smoke vapours.

From theoretical considerations[11] it seems likely that in these experiments particle deposition made very little contribution in the "smoking" of water due to the small size of the particles and to the relatively small area of water surface per unit volume of smoke. The geometry of the wet surfaces in the human lung is different from the system used in the experiments with wood smoke, and the relative contributions of particles and vapours will therefore be different. As already mentioned, the usual site of lung cancer is the bronchi, but this cannot be readily explained from considerations of the mechanism of the deposition of tobacco smoke particles.[9] However, it is likely that the rate of deposition of the vapours of smokes will be greatest in the wide tubes in the lung, such as the trachea and bronchi, since it is in these regions that the quantity of vapours available per unit area of absorbing surface is greatest. Although it might be argued that certain carcinogens such as 3:4 benzpyrene, being almost insoluble in water, would not be expected to be "scrubbed" from the vapour phase by moist surfaces such as bronchial epithelial tissues,[12 13] the work of Falk, Miller, and Kotin[14] on the desorption of 3:4 benzpyrene from soots by plasma proteins suggests that tissues may not behave as ideal systems. In view of these results of work on wood smoke and of the above discussion, it is suggested that it might be useful if further consideration were given to the relationship between lung cancer and the absorption by the lung of vapours from tobacco smoke and polluted air.—I am, etc.,

Torry Research Station, Food Investigation Organization, Department of Scientific and Industrial Research, Aberdeen. W. W. FOSTER.

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13. Simpson, T. H. (Torry Research Station, Aberdeen), personal communication, 1958.
14. Falk, H. L., Miller, A., and Kotin, P., *Science*, 1958, **127**, 474.

A Moral Obligation

SIR,—Having read the letter of Dr. A. Robinson Thomas (*Journal*, April 11, p. 972), I also am surprised at the absence of comment or supporting letters concerning the injustice to Mr. A. H. Barber by a regional hospital board (*Journal*, March 14, p. 702). I wrote to *The Times* on March 6 giving details of a similar injustice, but as my letter has not been published I hope that you can find the space to print the circumstances.

In January, 1958, Dr. S. Childs, the Scunthorpe Medical Officer of Health, had his part-time appointment as junior consultant in infectious diseases summarily cancelled by the Sheffield Regional Hospital Board, after 10 years of excellent work. His appeal to the Ministry was refused on a technical point. His popularity locally was such that a petition to the Minister for restoration of his services collected ten thousand signatures, including those of 12 medical practitioners.

The Central Consultants and Specialists Committee of the B.M.A. independently approached the Ministry on his behalf, opposing the action of the regional board in thus unnecessarily removing his specialized knowledge from the local hospital. On July 23, 1958, Mr. L. Mallalieu, Q.C., M.P., introduced a deputation to the Ministry of Health, when the protests, petition forms, and B.M.A. recommendations were formally presented to the Parliamentary Private Secretary.

Dr. Childs, on legal advice, issued writs against his alternative employers, the borough council and the county council, alleging wrongful dismissal. These have been settled out of court on the basis that his appointment was never properly terminated in law, and the defendants pay costs and his salary up to April 30, 1959.

Dr. Childs has still not been reinstated in his hospital post, and one consequence is that children with certain fevers such as poliomyelitis are now transferred 30 miles (48 km.) to Grimsby, whereas previously they were always treated locally and could be visited daily by their parents.

One very serious feature of this case is the fact that the letter from the secretary of the regional board giving three months' notice of dismissal was apparently sent and dated some days earlier than any entry in the minute book of any committee meeting of the board discussing or authorizing such action. Inquiry on this point was met with complete refusal of information on the grounds that the proceedings of the regional board are secret and privileged. This state of affairs is obviously dangerous and should be amended without delay.

The Minister of Health would be well advised to take a more critical attitude to the plausible explanations of incidents such as these, supplied by his permanent administrative staff, and to show initiative in finding ways and means of righting the more obvious injustices committed in his department.—I am, etc.,

Scunthorpe, Lincs. DAVID E. HOBDAY.

Prophylactic Tetanus Toxoid

SIR,—May I make a strong plea for greater publicity for the use of prophylactic tetanus toxoid? Although its advantages are generally known within the profession, one finds that relatively few patients are in fact protected in this way, and the difficult decision about the use of serum in casualty patients showing some reaction to a test dose of serum continues to be a source of anxiety for those responsible for the treatment of casualties. Even the use of serum when safe may sensitize the patient so that its use for subsequent injuries is difficult. The alternative use of toxoid appears to be so very simple and free of complications that a campaign for its more general adoption would appear to be justified.—I am, etc.,

Sevenoaks, Kent. R. PITTS CRICK.

Bacteria in Antiseptic Solutions

SIR,—Your annotation entitled "Bacteria in Antiseptic Solutions" (*Journal*, August 16, 1958, p. 436) draws attention to the danger of living bacteria in cetrimide solutions and the work of Lowbury,[1] who traced the contamination of the solution to bark corks: also the work of Anderson and Keynes,[2] who proved that the organism lived in the bark cork and that on removing the cork the organisms were deposited into the antiseptic where they survived for a period.

On October 15, 1958, a young primipara was given one pint (0.6 litre) of blood for post-partum haemorrhage. Nine hours later, despite energetic treatment along accepted lines, she died. An atypical colon bacillus was recovered from the small amount of blood remaining in the bottle used. It was also present in the antiseptic—cetrimide—used to swab the donor's arm. It survived in the antiseptic for 10 minutes. The same organism was also found in the cork of the antiseptic bottle. The sequence of events is thus clear. The organism entered the antiseptic from the cork and was transferred, with the antiseptic, on to the donor's skin. As the needle pierced the donor's skin, the bacilli present were collected and thus entered the donor blood. The bacillus grew readily at 4° and less readily as 37° C. was approached. Other bottles (eight) were found to be contaminated, but fortunately not used.

As a result of this happening it is considered that no antiseptic solution of any description which will come into contact with an eye, a surgical wound, or skin through which an incision or puncture is to be made should be stored in any container which is closed with a bark cork. The use of bark corks should be limited to closing vessels containing medicines and other preparations intended to be given by mouth.

It is suggested that the above sequence of events may have occurred in other reactions due to contaminated blood where the actual source of contamination was not found.

I wish to thank Dr. J. Quinlan and the laboratory technician, Mr. Jensen, for their help in ascertaining the source of contamination.

—I am, etc.,

Burnie, Tasmania. T. G. INGRAM.

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[2] Anderson, K., and Keynes, R., *Brit. med. J.*, 1958, **2**, 274.

Disposable Giving Sets

SIR,—Several types of plastic disposable blood-transfusion recipient sets ("giving sets") have recently been distributed to teaching and other large hospitals for use and comment.

As the representative of the Faculty of Anaesthetists on the subcommittee of the British Standards Institution which is considering blood-transfusion equipment, I would welcome any comments and criticisms regarding or suggestions for improvement of the disposable sets now in circulation. Perhaps readers who feel disposed to help in this way would write to the following address: Department of Anaesthesia, King's College Hospital,

London, S.E.5. Information supplied would be regarded as confidential and passed on to the committee anonymously after correlation.—I am, etc.,

A. H. GALLEY.

Pancreatitis

SIR,—We would like to comment on the paper of Mr. M. A. Birnstingl (*Journal*, April 11, p. 938). Over the past few years we have had under our care about 40 patients with chronic pancreatic disease, 20 of whom have had a variety of surgical treatments.

We feel that Mr. Birnstingl pays insufficient attention to recent investigative techniques of value in the differential diagnosis of chronic pancreatic disorders. There is little justification for comparing as equally chronic two disorders so different in their time relations as the two compared in his paper. One should not call the disease described under the first heading "chronic" pancreatitis when the average length of symptoms was only 7.6 weeks. True chronic relapsing pancreatitis develops over many years and rarely comes to specialist investigation until symptoms have been present for some years. There is, therefore, little justification for the author's first category of "chronic" pancreatitis, except that derived from a histological report, which, as the outcome of this group of cases showed, was obviously incomplete. We were struck with the apparent assumption of Mr. Birnstingl that the obstructive factor is inconsiderable in chronic relapsing pancreatitis. This is against current general opinion. The obstruction may be at the ampulla, but it need not necessarily be in any major duct, and may be far back in the gland. The recognition of the site of an obstruction or localized disease may be difficult at times, and is a major difficulty in surgery of some cases.

Our experience confirms Mr. Birnstingl's observations that alcohol is an unimportant aetiological factor. Alcohol undoubtedly can cause pancreatic disturbance in chronic alcoholism, and we have seen this not infrequently. In contrast to American experience, our Irish cases are frequently teetotallers, and this is true of the major cases.

We feel that the diagnosis of chronic disease of the pancreas may require, and usually does, a full battery of tests based upon careful clinical appraisal of the case, and supplemented by radiology. These tests will include careful faecal examination, faecal fat determination, radioiodine tagged triolein and oleic acid absorption curves (if available), glucose tolerance curves, and, especially, some variety of the secretin/pancreozymin test. We use Howat's serum test and are most satisfied with it. Other tests, such as vitamin A acetate and alcohol absorption curves, may be of occasional value.

Chronic relapsing pancreatitis is, we feel, not at all so uncommon as is generally assumed. It does not, *at first*, necessarily manifest itself as a major disturbance, but it usually does so eventually. We feel that many patients who manifest the lesser symptoms are missed because the diagnosis is not considered. We are, however, satisfied that with proper tests this diagnosis can often be made with considerable confidence years before it may be confirmed at operation, or by the development of an acute episode of pancreatic disturbance with the well-known features of that disturbance. In addition we feel that sphincterotomy may be of great value if the case is diagnosed early, while the later case with the marked changes arising from chronic obstruction may require excisional surgery. Finally, on a point of nosology, we feel that to call the disease "chronic relapsing pancreatitis" is frequently incorrect, for these patients very often demonstrate persistent, though often slowly progressive, symptoms. In other words the chronicity is evident, the relapse is rarely so notable. There are examples of the relapsing types, but they are in our experience infrequent. It should be remembered that the disease has perhaps a different aetiology (*vide* alcohol) here and in America. We feel that the term chronic progressive pancreatitis may be more useful and more descriptive.—We are, etc.,

OLIVER FITZGERALD.
PATRICK FITZGERALD.

St. Vincent's Hospital, Dublin, and
University College, Dublin.

Lumbar Puncture

SIR,—After reading your leading article on lumbar puncture (*Journal*, December 20, p. 1520) I consider it my duty to submit to you a little hint concerning the avoidance of headache after lumbar puncture. I read it some months ago in a German journal[1] and have tested it with satisfactory results up to now in a few cases. After the lumbar puncture (no matter whether for diagnostic or anaesthetic purposes) the needle should be withdrawn a little into the epidural space and 5–10 ml. of isotonic saline (0.9% NaCl) solution should be injected to prevent the leakage of C.S.F. by increasing the pressure in the epidural space. I hope that this simple procedure, if not yet known in Great Britain, may prove helpful.—I am, etc.,

Berlin. J. E. ROLLENHAGEN.

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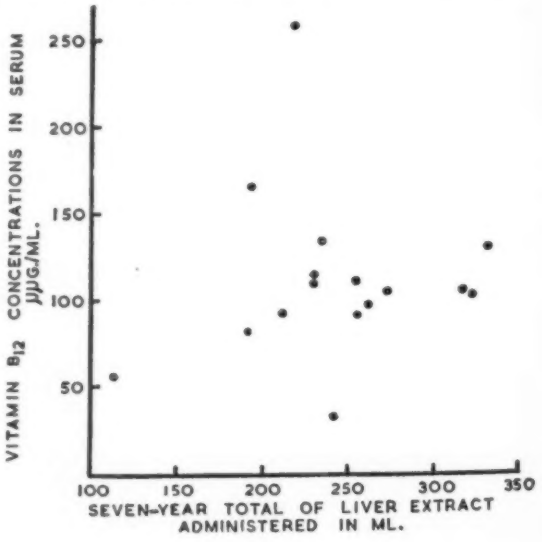
[1] Harrer, G., *Medizinische*, 1958, **29**, 1132.

Subacute Combined during Liver Therapy

SIR,—Drs. J. F. Adams and G. C. Timbury in their article (*Journal*, March 28, p. 833) illustrate the sad consequences resulting from the use of liver extracts of unknown potency. One cannot but agree with all the points they make.

We have recently been assaying (by the *Euglena* method) sera of patients who have been receiving injections of a "high potency" liver extract for a period of at least seven years. The total amount of liver extract administered over the last seven years corresponded roughly to the medium to maximum recommended by the manufacturers for maintenance therapy (2 to 4 ml. every four weeks = 182–364 ml. in seven years). In fact, during this period the patients received amounts varying from 112 to 328 ml. The



intervals between injections, however, were in some cases longer than 4 weeks (5, 6, or even 12 weeks).

From the Figure it can be seen that all but two of the 16 patients—randomly selected from a larger group of similarly treated individuals—had subnormal values of serum B_{12}. Six of the patients had serum concentrations less than 100 $\mu\mu$g./ml., and the one with the lowest level (36 $\mu\mu$g./ml.) had a relapse of megaloblastic erythropoiesis (Hb 8.6 g., P.C.V. 27%). Owing to an intercurrent illness, this latter patient had missed the last of her periodic injections before the blood count and assay.

The strength of this high potency liver extract was not stated by the manufacturers. An assay carried out by us gave an approximate B_{12}-content of 10 $\mu\mu$g./ml., making the seven-year total received by the patients 1,120 to 3,280 μg., which is well below the maintenance dose recommended by Mollin and Ross.[1]

From these observations it is obvious that it is highly important to know the vitamin-B_{12} content of any liver extract used, and to adjust the doses and intervals between the injections accordingly. Unless this is done, patients treated with liver extracts will find themselves earlier or later on the brink of a haematological relapse and/or of a neurological complication.—I am, etc.,

City General Hospital, Sheffield. S. VARADI.

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Children's Footwear

SIR,—A few years ago I was examining a 10-year-old girl at an orthopaedic school clinic. I noticed something most unusual about her feet; all her toes were perfectly straight! I am therefore not altogether surprised that Dr. Daphne Sasieni (*Journal*, March 14, p. 720) has failed to see a single child over 3 years old with ten straight toes.

No one doubts that badly fitting shoes can cause harm to schoolchildren's feet, and I would like to see shoe manufacturers make a real effort to vary their fittings, as at present they are quite inadequate, even in the most expensive footwear. Faulty shoes cause most damage to feet already affected by hallux valgus, hammer toes, and other deformities. I can never understand why it is difficult to believe that, just as the shape of the face and hands is inherited, so is the shape of the foot and toes. However, let us have a sense of proportion. Most deformities of the feet and toes are developmental, and it will be necessary to alter the genes rather than the child's footwear in order to prevent them.—I am, etc.,

Halifax. GEOFFREY HYMAN.

Early Diagnosis of Mental Defect

SIR,—In the correspondence between Dr. Brian H. Kirman (*Journal*, January 3, p. 50) and Professor R. S. Illingworth (*Journal*, November 29, p. 1355) on the subject of the early diagnosis of mental defect, Professor Illingworth has aptly made the points that a diagnosis of mental deficiency is not made on the basis of bad or abnormal behaviour but on the basis of a complete diagnostic evaluation, and that gross motor behaviour is not an adequate criterion of intellectual development. Although we feel it is inadvisable to make an unqualified diagnosis of mental deficiency to parents in the first year of life, there is one advantage to early evaluation of development with which Dr. Kirman would agree. It gives parents a reasonable guide for current expectations, so that the adverse environmental factors, either over-protection or pushing beyond the child's capabilities, will be minimized and the maximum potential of the infant more readily realized.

Beyond this, however, studies that we have done—the details of these examinations with a bibliography appear in the January, 1959, issue of *Pediatrics* in a letter to the Editor—indicate that when care is taken to eliminate bias and the infant examination is used as a clinical neurological tool by a physician adequately trained in its use, it is as satisfactory a predictor of later development as any psychological examination done at 3- to 7-year intervals. This approach of the Gesell Developmental Examination has not been employed by the psychologists who developed or used the tests which form the basis of the reports in the literature quoted by Dr. Kirman. They have been concerned rather with predicting precise I.Q.s in relatively homogeneous groups of infants. Ignoring the fact that infant behaviour as well as socially learned later behaviour both have their roots in the central nervous system, which operates throughout the life span of any individual, has led them to the erroneous conclusion that "infant testing" is invalid.

When the matter is approached from the medical viewpoint, correlations ranging between 0.5 and 0.75 between infant and later examinations have been found in four large groups of infants evaluated initially by the Gesell Developmental Examination and re-examined between 3 and 7 years of age. Gratifying as the predictability is, however, predicting school age I.Q. is not the major objective of the infant evaluation. Its two most important functions are, first, to make a diagnosis of the normality or abnormality of neurologic functioning, and, second, to detect those infants with a developmental potential that is below normal, usually on an organic basis. As clinicians we would feel that an examination which would allow us to make the following statement is an eminently acceptable and useful tool: "This infant has no neurologic impairment, and his potential is within the healthy range; depending on what his life experiences are between now and 6 years of age, he will at that time have a Stanford–Binet I.Q. above 90, unless qualitative changes in the central nervous system are caused by noxious agents, or gross changes in *milieu* alter major variables of function."—I am, etc.,

Clinic of Child Development, The Children's Hospital, Columbus, 5, Ohio. HILDA KNOBLOCH.

REFERENCE

[1] Knobloch, D., *Pediatrics*, 1959, **23**, 175.

Medicine on Television

SIR,—I feel I must comment on the unsuitability of recent television dramas on a medical theme. In the past few months we have witnessed such specialized procedures as corneal grafting, replacement transfusion in erythroblastosis, and a rather disrespectful necropsy, amongst other things.

Whilst a certain amount of education of the public is very salutary, such medical technicalities do *not* constitute an evening's entertainment, and I feel that the choice of such subjects only undermines the vital relationship between the patient and his doctor and also confuses the attitude of the patient to his illness. Let there be well-informed documentaries, by all means, for the discerning viewer, but surely there should be stricter

control over the choice of subject matter in these plays with a mass audience.—I am, etc.,

Blackheath, Near Birmingham. NANCY M. BOSC.

Subject in Search of a Name

SIR,—The *Journal of the American Medical Association* for April 4, 1959, contains a delightful editorial by A. L. Bloomfield on the origin of the term "Internal Medicine." It is a pity we cannot find some equally convenient name for the subject variously known as public health, epidemiology, social medicine, human ecology, population pathology, or group medicine, in which a collection of patients is studied. Medical surveys, follow-ups, and therapeutic trials are all part of "Great Medicine," as Alan Gregg called it, and we need a distinguishing adjective for them that is less equivocal than "social" or "group." Perhaps you could open your columns for more attractive suggestions.—I am, etc.,

Radcliffe Infirmary, Oxford. L. J. WITTS.

POINTS FROM LETTERS

Aetiology of Disseminated Sclerosis

Dr. S. S. JHAVERI (Nelson, Lancs) writes: It was most interesting to read the comprehensive and thought-provoking review of Drs. H. Miller and K. Schapira (*Journal*, March 21, p. 737, and March 28, p. 811) and your valuable annotation in the *Journal* of March 28 (p. 839). It is possible that certain further observations and self-questioning might help to achieve a greater insight of the aetiology of the disease process. It is beyond doubt that the condition is rarer in the tropical countries than in those with a cold or temperate climate . . . . If one considers multiple sclerosis as a hypersensitive disorder like acute disseminated encephalomyelitis, acute haemorrhagic leuco-encephalitis, etc., how would one explain the rarity of one in the tropics but not the others? The clinical and pathological features of the neurological syndrome which occasionally follows rabies and other viral inoculations are remarkably reminiscent of those seen in disseminated sclerosis, but then why is it that, if thought to be of the same aetiology, the former is far more common in the tropics than the latter?

Carcinomatous Arthropathy

Dr. MICHAEL KELLY (East Melbourne, Australia) writes: Dr. James D. E. Knox (*Journal*, February 28, p. 587) forbids me to record the fact that chronic polyarthritis began a few days after an operation. This is not a "clinical impression"; it is a fact. And I have seen a dozen such facts in the past three years. Yet (says Dr. Knox) they must be suppressed in view of the common belief that rheumatoid arthritis is a clinical entity whose cause is unknown. . . . I am not overwhelmed by the authority of the Empire Rheumatism Council's Scientific Advisory Committee (*British Medical Journal*, 1950, **1**, 799). They used statistical methods, which are notoriously misleading in discovering the truth about uncommon factors and about the cause of polyarthritis in any individual patient. . . . According to their report, moreover, no questions were asked about operations and injuries occurring a few days before the onset of polyarthritis. In a few patients the answers to these would have been "yes" and would have been difficult to explain. Similarly, any questions about coincident skin troubles, neurological disease, or lung cancer would have been futile, because all arthritic patients with these disorders had previously been excluded (arthropathy and not arthritis). And there is no mention of urethritis, a known cause of arthritis which we must not call rheumatoid. The labours of the Committee were founded on the outworn belief in the single causation of disease. The answers were yes or no, and no provisions were made for multiple causation in which two or more factors played a part.

Obituary

JOHN HAY, M.D., F.R.C.P.

Professor John Hay, emeritus professor of medicine in Liverpool University, died at his home at Bowness-on-Windermere on April 21. He was 85 years of age.

John Hay was born at Birkenhead on November 25, 1873, the son of an architect. Educated at the Liverpool Institute and at University College, Liverpool, which at that time was a constituent college of the Victoria University of Manchester, he qualified by taking the London Conjoint diploma in 1895. In the following year he obtained the Manchester degrees of M.B., Ch.B., with honours, proceeding to the M.D. in 1901 with a commendation for his thesis. He had a brilliant record as a student, gaining medals in anatomy, physiology, and medicine, and the Holt fellowship in anatomy and surgery. In 1904 he was granted the degree of M.D. of the newly established University of Liverpool. Elected a Member of the Royal College of Physicians of London in 1903, he was admitted a Fellow of the College in 1915.

[*Burrell and Hardman, Ltd.*

After qualification Hay held the appointments of house-surgeon at the Liverpool Lock Hospital, house-physician at Liverpool Royal Infirmary, and assistant (later, senior assistant) medical officer at the Mill Road Infirmary, Liverpool. From 1900 to 1903 he was medical tutor and registrar at the Royal Infirmary, and during the next few years he was appointed to the staffs of several hospitals in and near Liverpool. In 1907 he became an assistant physician at the Liverpool Royal Infirmary and about ten years later full physician.

During the first world war he served in France with the R.A.M.C., ultimately becoming officer commanding the medical section of the 57th General Hospital, with the rank of lieutenant-colonel, and serving as a specialist in cardiac disorders in the Western Command. After the war he was appointed honorary consulting physician to the Ministry of Pensions. In 1924 he succeeded Professor J. Hill Abram as professor of medicine in Liverpool University, and he held the chair for ten years, being appointed professor emeritus on his retirement. His fame as a cardiologist spread far beyond Liverpool. In the Royal College of Physicians of London he was Bradshaw lecturer in 1923 and some years later he served on the council of the College. He chose coronary thrombosis as the subject of the St. Cyres lecture, delivered at the National Hospital for Diseases of the Heart in 1933. Three years later he gave the Strickland Goodall memorial lecture at the Society of Apothecaries of London, speaking this time on thyrotoxicosis and heart disease. He was an honorary fellow of the Royal Society of Medicine and an honorary member of the British Cardiac Society. At the Annual Meeting of the B.M.A. in 1922 he was a vice-president of the Section of Medicine.

In Liverpool he took a very active part in medical affairs. He was an ex-president of the Liverpool Medical Institution and of the Microscopical Society. He edited the *Liverpool Medico-chirurgical Journal*, and, an artist of some distinction himself, he was at one time president of the Liverpool Sketching Club. A justice of the peace for the City of Liverpool, he was later made a deputy lieutenant

of the County Palatine of Lancaster. He had lived at Bowness-on-Windermere since his retirement.

In 1906 he married Agnes Margaret, daughter of Dr. William Duncan, of Tyldesley, Lancashire, and had two sons and two daughters. He was left a widower in 1947. One of his sons is the professor of child health in Liverpool University

We are indebted to Lord COHEN OF BIRKENHEAD for the following appreciation:

John Hay was a resident in the Liverpool Royal Infirmary before any present member of the staff was born, yet when he retired 25 years ago he was as young as any of us in appearance and spirit. He grew old but never lost life's zest. He was the ideal physician, skilled in the science of medicine and a supreme master of its art. From him patients drew strength and courage. His serenity and equanimity in the sick room or hospital ward inspired confidence, and his lively personality, charm, and wit radiated an irrepressible optimism. He was a model teacher. His style was simple and direct, and the stories which enlivened his lectures had more than local fame. Unlike many of his contemporaries in the earlier years of this century, he grasped the opportunities which newer methods of investigation offered. He worked with Sir James Mackenzie and made notable contributions to the literature of heart disease. He founded in the Royal Infirmary one of the first and finest provincial heart centres, and the prestige and status of the Liverpool school of cardiology stem from his outstanding work. From the day of his appointment as Professor of Medicine in the University of Liverpool in 1924, he threw himself whole-heartedly and with his accustomed energy into its academic life, and when ten years later he retired his students and colleagues showed by the gift of a portrait and in other ways their warm gratitude and affection.

Honours, both local and national, were showered upon him. He was President of the Liverpool Medical Institution and a deputy lieutenant of the County Palatine of Lancaster; he was President of the Cardiac Society and of the Association of Physicians; and he was accorded the rare distinction of Honorary Fellowship of the Royal Society of Medicine. His commanding position in cardiology was recognized by his appointment as regional adviser in medicine and specialist in cardiac diseases to Western Command and Ministry of Pensions. He gave the Bradshaw Lecture in the Royal College of Physicians, and later delivered the St. Cyres, James Mackenzie, and Strickland Goodall lectures. Moreover, he was one of the first to stress the importance of social medicine, and he strongly supported temperance and smoke abatement movements.

John Hay had an immense capacity for friendship. Whether in the 1st Western General Hospital in France in the first world war, in hospital, at the Medical Institution, the Association of Physicians, or with his travelling medical club, he always had around him a host of admiring young friends fascinated by his gifts as raconteur and mimic. And after he retired to Windermere he was the most welcome guest at the meetings of the British Paediatric Association which were held in the Lake District. But his interests were not confined to medicine. He was a man of wide culture and many facets. He had inherited artistic gifts from his father, who was a distinguished Liverpool architect, and John's brother, Hamilton, had a national reputation as a painter. John himself was an ex-President of the Liverpool Sketching Club, and his water colours adorn the walls of many of his friends. But among their most prized mementos are the sketches he made on agenda papers or menu cards during many a boring meeting or meal. He played the violin, as he did all else, with unbridled enthusiasm and verve. He rarely missed a Philharmonic concert, but he preferred the more intimate charm of chamber music. When he retired to Windermere he found great happiness in his garden until blindness shut out the colours he loved so well. And there in the Sabbath of his days he could rejoice in the success of both his sons, who have so distinguished themselves in medicine, and continue to enjoy the company and unrestrained affection of his many friends.

To me John Hay's passing is the end of an era. Forty years ago he was my teacher; thirty-five years ago I became a junior colleague on the staff of the Royal Infirmary; and twenty-five years ago I succeeded him in the Chair of Medicine. No one could have had a more loyal and helpful master and friend, or a wiser counsellor. He was devoid of malice and guile. From him I received never-failing encouragement in many troubles and perplexities. His tact, integrity, and selflessness were seen in many delicate and successful hospital negotiations. In committee his sense of fairness, his ability to grasp the core of the problem and, often by his intuitive understanding of people and things, to solve it, led to his being our accepted leader; but in this role he never sought to dominate; his sole aim was to help. Nor shall we forget his restless energy—

> "The heights by great men reached and kept
> Were not attained by sudden flight
> But they, while their companions slept,
> Were toiling upward in the night."

For fourscore years his frame, his heart, and his spirit were young. Then slowly old age crept upon him—that old age which is, as Seneca tells us, an incurable disease. But his courage and spirit never aged; to the end they remained invincible. Now he has passed on beyond our mortal vision. We shall hear no more the voice of one we loved so dearly. But his place in the history of English medicine is secure. May we not say of him as Pericles said of the Athenian dead: "When great men die, the whole earth is their memorial. Stone monuments may record their praises. But everywhere their fame lives on in the hearts of men, as in a cenotaph not made with hands." A beloved physician, a vital and unforgettable personality, a warm and trusted friend, John Hay is for ever enshrined in our hearts. May he rest in peace and light perpetual shine upon him.

A. C. ALPORT, M.D., F.R.C.P.

Dr. A. C. Alport, formerly professor of medicine at Cairo University, died in St. Mary's Hospital, Paddington, on April 17. He was 79 years of age.

Arthur Cecil Alport was born in South Africa, where his father worked in a family business. For his medical education he came to Edinburgh, graduating M.B., Ch.B., in 1905. Returning to South Africa, he practised in Johannesburg with his brother-in-law, and owned a gold mine, which unfortunately for him became a non-producer. During the first world war he served in the R.A.M.C., first in German South-West Africa and later in Salonika. In between these two periods he was in England, working as a specialist in medicine at the Royal Herbert Hospital, Woolwich. During his service he gained great experience in the treatment of malaria, and his book on the subject was published after the war.

On demobilization he proceeded to the M.D. at Edinburgh in 1919 and took the M.R.C.P. of London in the following year. In 1922 he became one of the staff of the medical unit at St. Mary's Hospital and he remained there for the next 14 years. One of his main clinical interests was in nephritis, on which he wrote a textbook, published in 1929. This third book, *The House of the Curious*, was a volume of family reminiscences.

Dr. Alport went to Cairo as professor of clinical medicine in 1937, the year in which he was elected F.R.C.P. He was also director of the medical unit at King Fuad I Hospital. In 1944 he sent in his resignation from his appointments in Cairo in order to draw attention to the abuses which existed in the hospitals—such as, the demanding of bribes by the nurses and the ill-treatment of the poorest patients. His resignation was eventually accepted after several efforts had been made to persuade him to withdraw it.

Dr. Alport married Janet, youngest daughter of James McCall. She survives him, together with his only son, Mr. C. J. M. Alport, M.P., Parliamentary Under-Secretary of State, Commonwealth Relations Office.

We are indebted to Professor F. LANGMEAD for the following appreciation: I first met Dr. A. C. Alport during the first world war in Salonika, where he had got into the black books of the D.M.S. and other high officials for his outspoken and downright criticisms of the tardy adoption of intravenous quinine injections for cerebral malaria, a method of treatment which he claimed to have found very successful. After the war he returned to Britain, and on the formation of the medical unit at St. Mary's Hospital Medical School he became second assistant to it (subsequently to become assistant director). Knowing of his previous career and his downright and forcible character, I had some misgivings, but they proved to be quite unfounded and we worked together in perfect amity and friendship. He was absolutely loyal throughout the tenure of his appointments. His teaching—which comprised chiefly the method of examination of patients and the import of the signs elicited—was much appreciated by the students, as was his friendly comradeship with them. I shall always be grateful for his support and unfailing help at St. Mary's, and am sure that many old students will look back with gratitude to his friendship and teaching.

W. H. H. writes: I knew A. C. Alport originally from the wrong side of the examination table, and later for some years in Egypt, where he was professor of medicine to the University of Cairo. His simple clarity of thought, his unswerving pursuance of what he had decided was the correct path, and a sense of humour which was never quite overlaid by whatever he was preaching at the moment, were a few of the facets of his character which endeared him to his friends, colleagues, and students. He was outspoken, but with the conviction that he was right, and always ready to review and, if necessary, recast his ideas.

Essentially a crusader, he very soon became respected and loved by his Egyptian students not only for the sincere and conscientious way he taught them textbook and bedside medicine but also for the improvements in their conditions, which were often the result of his campaigns in the Senate. As a colleague he could always be relied upon to advise, and although in principle he would never see a patient ("There are plenty of my Egyptian colleagues") in practice he would always give you the benefit of his long and varied experience.

His interest in the welfare of his students spread to that of his patients, for whose social betterment he was always campaigning against the Government. Finally, in desperation, he wrote his famous Black Book, and had it printed and distributed himself. His exposure of the corruption which existed in the Egyptian hospitals sparked off a long-needed revision of the hospital administration. His temporary unpopularity with his colleagues and the storm of newspaper criticism tested his patience and temper. From the storm he finally emerged more popular than ever with his colleagues and a benefactor to the poor Egyptian.

Perhaps his greatest outside interest was golf—a subject on which he had much to say. It was not very surprising to pass the practice ground at Gezira during the Open Championship and to find Alport laying down the law to Bobby Locke or Dai Rees with the same persistent conviction that he brought to the rest of his activities.

H. M. HARWOOD, M.B., B.Chir.

Mr. H. M. Harwood died at his home in St. John's Wood on April 20, aged 85. After graduating in medicine he went into business, and later became well known as a playwright. Over a period of more than 30 years he had many plays produced on the London stage, and several of them were notably successful.

Harold Marsh Harwood was born in Eccles, Lancs, on March 29, 1874, the son of George Harwood, at one time Member of Parliament for Bolton. He was educated at Marlborough College, Trinity College, Cambridge, and St. Thomas's Hospital, where he was a junior by a year or two to Somerset Maugham. Graduating M.B., B.Chir. in 1900, he held the appointment of house-physician at his teaching hospital, but after practising for a short time in the city he gave up the practice of medicine, except for the duration of the first world war, when he served as a captain in the R.A.M.C. in France and Egypt. His business interests were in cotton, and he became managing director of Richard Harwood and Sons, and chairman of Fine Cotton Spinners' and Doublers' Association.

Harwood's career as a playwright began before the first world war, but his first considerable success was *Please Help Emily*, produced in 1916, with Charles Hawtrey and Gladys Cooper in the cast. In the following year he collaborated with Miss F. Tennyson Jesse in writing *Billeted*, a farcical comedy which was revived in 1926. Harwood married Miss Tennyson Jesse in 1918. They wrote several plays together, including *A Pin to See the Peep-Show*, which, written around the Thompson–Bywaters case, was refused a licence for public performance in London, but was put on by a theatre club in 1951.

Harwood went into theatrical management in 1920, becoming lessee and manager of the Ambassadors Theatre, but he gave this up in 1932, protesting that entertainment tax was too severe. In that same year two of his plays had first performances on successive nights, one with Gladys Cooper in the cast and the other with Marie Tempest. He wrote about twenty plays, among them *The Man in Possession*, *The Grain of Mustard Seed*, *So Far and No Father*, *A Social Convenience*, *The Transit of Venus*, and *The Old Folk at Home*. He also wrote the libretto for Sir Thomas Beecham's production of *Figaro*, and for a time he worked in Hollywood as a script writer. During the second world war he was co-author with his wife of two books about London, *London Front* and *While London Burns*. Miss Tennyson Jesse died last year. They had no children.

Medical Notes in Parliament

THE LORDS ON LIPSTICK

Lord DOUGLAS OF BARLOCH asked in the Lords on April 22 what azo or other synthetic dyes were used in the manufacture of lipstick; what research had been done on the cumulative toxicity of such dyes and with what results; and whether any control was exercised over the use of them for this purpose.

Lord CHESHAM, replying, said he understood that many synthetic dyes had been used in lipstick manufacture for a long time. So far as he was aware, no research had been undertaken on behalf of Her Majesty's Government into the toxicity of the dyes used for this purpose. If Lord Douglas had reason to think that any particular lipstick was toxic perhaps he would let him know.

Lord DOUGLAS asked if Lord Chesham was aware that the Food and Drug Administration of the United States had recently banned no fewer than 17 synthetic dyes for use in lipstick; and was it not well known that many of these synthetic dyes were cancer-inciting? Lord CHESHAM said he was not aware of any action by the American Government because, so far as he knew, they had not done anything further than produce a proposal to ban 17 dyes. This was very much in the early proposal stages and was far from any form of firm decision.

Lord DOUGLAS asked whether it was not the fact that the action taken in the United States was based upon

research? Lord CHESHAM: It may well be, but, so far as I know, the problem which the noble Lord has raised is a new one.

MENTAL HEALTH BILL THROUGH COMMITTEE

The standing committee has completed its examination of the Mental Health Bill and returned it to the House. The 17 sittings, taken together, must constitute one of the better pieces of Parliamentary work. They have been singularly free from the party approach, they have been imbued with a common desire to fashion a good piece of work, and while opinions have been firmly held and forcefully expressed—for example, on the justifiable limits to restraint on personal liberty—there has been a notable absence of personal rancour and party contention.

There is a lot of tidying up to be done on the report stage, and some substantial pieces of administration to be put into shape. The final meeting of the committee on April 21 seemed to have a rather hurried air about it. That was due to the loss of two days that would have been available in the ordinary working routine but for the occurrence of Easter and the Budget.

Directions to Local Authorities

A new clause which the MINISTER OF HEALTH moved on the last day took the committee right back to the beginning of things. Entitled "Commencement," it gave effect to a promise he made at the fourth sitting that he would propose any drafting amendment required to enable him to give directions under Sections 20 and 28 of the National Health Service Act to impose on local authorities an effective obligation to carry out their duties.

The new clause, as the Minister explained it, provides that the Bill shall come into operation on such date as he may, by order, appoint. The general authority to start the wheels moving operates immediately on the Royal Assent. Different dates may be appointed for different parts of the Bill; and the Minister is given express power to give a direction, as soon as the Bill is passed, converting into duties the functions under Section 28 of the 1946 Act, as clarified by Clause 6 of this Bill. These are functions of local health authorities relating to the prevention of illness and the care and aftercare of patients. It is intended, the Minister explained, very quickly after the Bill receives the Royal Assent, to issue a direction defining the duties of local authorities, and a further direction, accompanied by detailed guidance, requiring them to submit proposals within a period of possibly six months.

Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.) asked him to stress in the directions the form of co-operation between the local authorities and the general practitioners and the hospital staff in tackling the provision of community services. The general practitioner would have to play a much bigger role than in the past, and it was important that this work should link up with the local authority view. Mr. D. WALKER-SMITH assured him that he had the point very much in mind, and when he addressed representative bodies, or when he was perhaps more agreeably engaged in informal discussion with members of the profession, he stressed it strongly. The clause was agreed to.

Composition of Review Tribunals

Mr. KENNETH ROBINSON (St. Pancras North, Lab.) sought to insert in the First Schedule (Mental Health Review Tribunals) a specific provision that the medical members of the tribunals could include psychiatrists. He withdrew it after the Minister had pointed out that, while in the ordinary way most of the medical practitioners on the tribunals would have psychiatric qualifications, there might be occasions when it was appropriate to have general practitioners and local authority doctors; for that reason the wider form of drafting was necessary.

Dr. DONALD JOHNSON (Carlisle, Con.) similarly wanted by another amendment to ensure that there should be a lay "and consequently to some extent unprejudiced" member on the tribunal. Again the Minister said that in the majority and normal run of cases things would be as Dr. Johnson wished, but that because of the possible exceptional case he would prefer the Bill as it stood. This amendment also was withdrawn.

It emerged during the discussion that the Minister was contemplating tribunals of three, and that, as Mr. K. ROBINSON put it, there might be occasions when the Minister would prefer two medical members. This would exclude the lay member. The balance of medical, legal, and lay thought was exceedingly important and ought to be preserved. He asked the Minister to think again about this. Mr. WALKER-SMITH agreed to see, before the report stage, if the principle of the presence of lay members on the tribunals could be preserved. He was sure the right number was three, but the figure was not sacrosanct. It might well be that on occasion the number should be exceeded so as to have a lay member; on some occasions it might be advantageous to have two medical members.

He also undertook to examine the possibility of confusion arising from the use of the same word, "tribunal," to describe the large regional tribunal of 12 or 15 persons, and the small body of three, although on the analogy of the Lands Tribunal, which sat in divisions also known as the Lands Tribunal, he saw no reason for confusion.

QUESTIONS IN THE COMMONS

Terry Dene's Medical Boarding

Mr. SYDNEY IRVING (Dartford, Lab.) asked the Minister of Labour on April 22 if he was satisfied with the way in which medical boards were operating in respect of national servicemen, in view of the case of ex-Rifleman T. Williams; and if he would make a statement. Mr. IAIN MACLEOD replied: Yes, I have the fullest confidence in the skill and judgment of medical boards set up under the National Service Acts. The boards consult specialists in cases of doubt and any man who thinks he has been wrongly graded may appeal.

Mr. IRVING said the public would not be able to see the logic of a man being found fit for service one day and fit for discharge the next. In view of these cases, would the Minister look at the system again? Mr. MACLEOD replied that he would look at the methods, but he found nothing surprising in the fact that medical men differed. The ordinary composition of the board was a chairman and four doctors, who called in consultant advice. In this case they considered the advice of two consultants. It was quite a long time later, and in quite different circumstances, that other doctors came to a different conclusion.

Lieutenant-Colonel J. K. CORDEAUX (Nottingham, Central, Con.) asked the Secretary of State for War what was the medical category of Rifleman T. Williams at the time of his enlistment on January 22, 1959; and on what medical grounds he was discharged from the Army as unfit for military service two months later. Mr. G. NABARRO (Kidderminster, Con.) also asked what was the medical grading of ex-Rifleman T. Williams, professionally known as Terry Dene, on first attestation into the Army; and for other details.

Mr. HUGH FRASER, Under Secretary, War Office, replied that Rifleman Williams reported for duty on January 22, having been placed in Grade I at his pre-service medical examination. When his Army examination took place on January 23 the unit medical officer found no reason to disagree with this grading. Williams reported sick on the following day and was admitted to hospital. The total cost of Rifleman Williams to Army Votes was about £100, his treatment in a civil hospital being provided by the National Health Service.

Slur on Boards Resented

Lieutenant-Colonel CORDEAUX said the rejection or immediate release from the Forces on medical grounds of people earning big money—T.V. stars, racing-car drivers, or first-class cricketers—caused great resentment among ordinary young men. As a result of these cases they and their parents were losing faith not merely in the efficiency but in the integrity in some cases of the medical boards concerned. Mr. FRASER answered that there was absolutely no question about the integrity of the medical boards. He resented that slur on the board. These cases were few, and when they fell on famous figures there was immense publicity. In this case the War Office was satisfied that what was done was done correctly.

Mr. J. STRACHEY (Dundee, West, Lab.) said in subsequent exchanges that what caused public anxiety was that these men were passed fit for service by one set of medical authorities and then sometimes within a very short period were found unfit by another set of medical authorities. How did the Under-Secretary account for that? Mr. FRASER: I account for it by the fact that if it is a psychiatric case, as this proved to be, the circumstances change very swiftly, and the final evidence which we have from the civil and military doctors is to the effect that this man is unfit to be a soldier.

Tonsils and Adenoids

Mr. J. CRONIN (Loughborough, Lab.) asked the Minister of Health on April 21 for statistics about the number of ear, nose, and throat consultants, registrars, clinical assistants, and house-surgeons employed in the Health Service in 1958; the proportion of their time devoted to tonsils and adenoids affections; how many operations were performed, and how many patients died; and the approximate cost incurred by the Ministry for persons suffering with these affections, exclusive of medical salaries.

Mr. D. WALKER-SMITH supplied the following details about medical staff holding E.N.T. appointments at December 31, 1957 (in whole-time equivalents)—

Consultants	222
Senior Hospital Medical Officers	16
Senior Registrars	33
Registrars	77
Senior House Officers	56
Junior Hospital Medical Officers	6

It was not possible, he stated, to distinguish time spent on treatment of affections of the tonsils and adenoids. The great majority of the 178,000 patients treated in 1958 in hospital beds set aside for the surgical treatment of tonsils and adenoids were likely to have had operative treatment. The number who died was not known, but provisional figures from the General Register Office indicated that during the year mention of a tonsil and adenoid operation was made on 33 death certificates. The cost of treating these patients was not separately identifiable.

Brucellosis in Cows

Sir GERALD WILLS (Bridgwater, Con.) asked the Minister of Health on April 23 to what extent damage to human health could arise from brucellosis melitensis in cows, either through the milk from such cows or any form of contact with the infected animal itself.

Mr. WALKER-SMITH stated that organisms indistinguishable in the laboratory from *Brucella melitensis* had been isolated from dairy herds in this country from time to time over the last twenty years, but no cases of human disease were known to have been caused. In the Mediterranean area a type of undulant fever, which was often a serious disease, was due to this organism and could be contracted from infected milk or by contact with infected material. Medical officers of health had powers in Regulation 20 of the Milk and Dairies (General) Regulations, 1959, to require heat treatment of milk infected with *Brucella*, and so make it safe.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **April 11** (No. 14) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire

CASES	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	2	0	4	0		2	0	2	0	
Dysentery	906	122	129	10	6	1,110	119	180	12	18
Encephalitis, acute	2	0		0		6	0		0	
Enteric fever:										
Typhoid	0	0	0	0		5	0	0	0	
Paratyphoid	22	13	1(B)	0		0	0	1(B)	0	1(B)
Food-poisoning	366	37	19	1		156	14	17	0	
Infective enteritis or diarrhoea under 2 years				13	26				7	19
Measles*	22,811	1376	598	437	380	4,165	250	113	26	10
Meningococcal infection	20	4	12	0	5	22	3	17	2	3
Ophthalmia neonatorum	31	0	5	0		35	35	4	0	
Pneumonia†	692	33	228	41	28	534	43	233	25	4
Poliomyelitis, acute:										
Paralytic	14	2	0	1		9	1	0	0	
Non-paralytic	5	0	0			0	0			
Puerperal fever§	222	32	15	0		161	18	5	1	
Scarlet fever	689	48	55	28	26	857	54	62	33	22
Tuberculosis:										
Respiratory	685	68	80	20		466	47	140	13	
Non-respiratory	54	4	14	0		40	5	8	1	
Whooping-cough	634	23	42	60	118	515	30	37	7	16

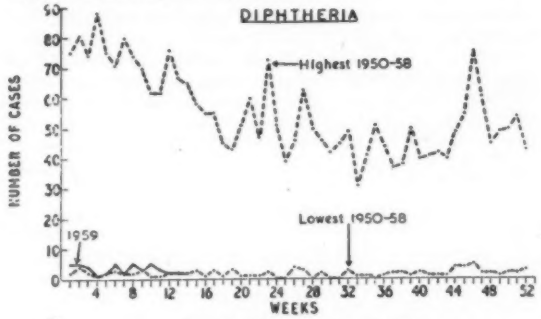
DEATHS	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	2	0	3	0	0	6	0	2	0	3
Influenza	206	3	10	7	13	46	3	6	1	0
Measles		1	1	0			0	0	0	0
Meningococcal infection		1	1				0	2		
Pneumonia	746	50	27		27	761	64	38	16	7
Poliomyelitis, acute	2	0		0	0	4	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	81	6	6	0	7	95	5	2	3	0
Non-respiratory		1	0	0	1		0	0	0	0
Whooping-cough	1	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	314	30	37	10	14	324	27	28	7	
Deaths (excluding stillbirths)	10,703	788	660	187	246	11,374	892	680	134	153
LIVE BIRTHS	15,867	1309	992	300	376	13,395	1112	935	249	341
STILLBIRTHS	346	21	26			312	20	20		

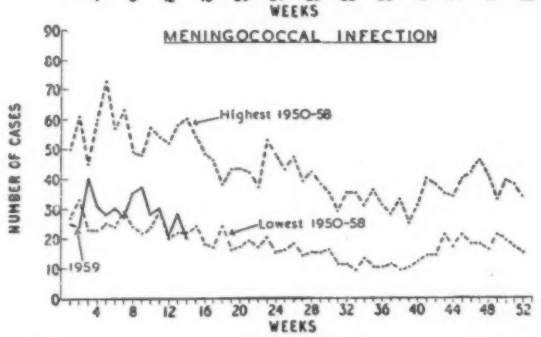
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

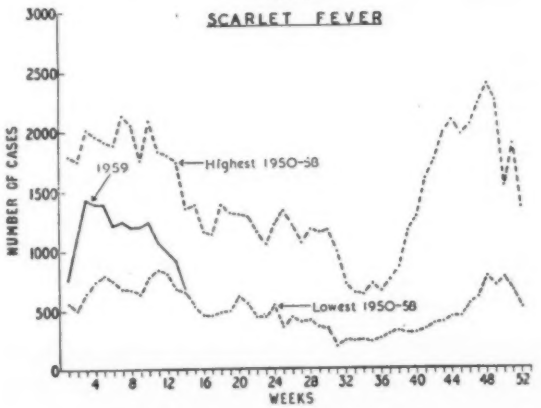
Vital Statistics

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus ------, the figures for 1959 thus ———. Except for the curves showing notifications in 1959, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







High Birth Rate in First Quarter

More births were registered in England and Wales in the March quarter than in any other quarter for 10 years. They numbered 191,699, giving a rate of 17.2 per thousand population. This was the highest rate for any quarter since 1949, when the rate for the March quarter was 17.3. The infant mortality rate was 24.7 per thousand live births; this was 0.7 lower than the rate for the March quarter of 1958 and 15.7 lower than the rate for the corresponding quarter of 1949.

Deaths registered in the March quarter numbered 176,901, giving a rate of 15.9 per thousand population. This is the highest rate for any quarter since the March quarter of 1951, when the rate was 19.1.

The stillbirth rate was 21.4 per thousand live and still births, the same as last year.—*Registrar-General's Weekly Return* No. 15.

Week Ending April 18

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available:

	Week Ending April 11	Week Ending April 18
Measles		
Berkshire	412	**377**
Reading C.B.	140	**121**
Devonshire	390	**266**
Plymouth C.B.	184	**173**
Durham	1,187	**1,088**
South Shields C.B.	134	**150**
Sunderland C.B.	245	**280**
Essex	1,784	**1,220**
Southend on Sea C.B.	271	**164**
Basildon U.D.	237	**106**
Hornchurch U.D.	107	**107**
Gloucestershire	595	**337**
Bristol C.B.	232	**141**
Kent	1,125	**884**
Orpington U.D.	188	**124**
Lancashire	1,855	**1,515**
Liverpool C.B.	157	**143**
Manchester C.B.	319	**363**
St. Helens C.B.	115	**107**
London	1,376	**972**
Lewisham	148	**111**
Wandsworth	160	**107**
Staffordshire	868	**719**
Stoke on Trent C.B.	116	**136**
Surrey	1,428	**981**
Croydon C.B.	313	**210**
Warwickshire	1,144	**1,051**
Birmingham C.B.	739	**504**
Coventry C.B.	98	**179**
Glamorganshire	450	**340**
Cardiff C.B.	210	**133**
Acute Poliomyelitis		
Hampshire	2	**3**
Southampton C.B.	2	**2**
Lancashire	0	**4**
Liverpool C.B.	0	**3**
Dysentery		
Essex	26	**30**
Gloucestershire	14	**19**
Bristol C.B.	11	**15**
Lincolnshire	51	**61**
Grimsby C.B.	26	**47**
Middlesex	59	**40**
Ealing M.B.	3	**10**
Northumberland	19	**27**
Newcastle upon Tyne C.B.	7	**11**
Surrey	30	**64**
Croydon C.B.	5	**16**
Surbiton M.B.	7	**23**
Worcestershire	81	**20**
Evesham M.B.	3	**12**
Evesham R.D.	70	**2**
Yorkshire West Riding	80	**84**
Barnsley C.B.	4	**12**
Bradford C.B.	19	**12**
Leeds C.B.	32	**35**
Glamorganshire	**38**	**42**
Cardiff C.B.	15	**23**
Rhondda M.D.	11	**10**

Medical News

The Church, Morals, and Medicine.—Writing in the *Canterbury Diocesan Notes*, the Archbishop of Canterbury, Dr. FISHER, referring to the partnership between the Churches and the profession, says:

"I could illustrate this thesis in several ways: at the moment I am thinking of the medical profession especially. There has always been a natural and inevitable affinity between the Church and the medical profession, since their ministries of healing cannot be separated: but it had come to appear to many people that in their partnership the one was scientific and authoritative and the other sentimental and subsidiary. There is in many quarters a renewed sympathy between the two and a recognition that in many ways neither can do the perfect work of healing without the co-operation of the other.

"The medical contribution to and reception of the Report on the Church's Ministry of Healing is evidence of this readjustment, though there are still, of course, many clergymen, many doctors, and particularly many psychiatrists who do not realize the absolute necessity of a full partnership. On neither side of the partnership is there infallibility; neither can dictate to the other; but in their joint pursuit of spiritual and physical health, they need each other. And this is especially so when they deal from either side with questions that are as much or more moral than medical. A doctor is perfectly free to publish an article disagreeing with the Church's view of fornication or other moral aberrations. But great injury to both sides of the partnership results, unless he makes it clear that he does not speak for his profession and that the fact of his being a doctor does not give him any special competence to deliver judgments on moral questions.

"Or again, whatever may be thought of A.I.D., the fact that some doctors had been practising A.I.D., knowing that it involved the parents in a false entry in the birth certificates, and that it raised many other legal, social, and moral questions, without seeking any formal advice from the Church or the legal profession or their own profession, injured the partnership. It is always serious to take the law, moral or civil, into one's own hands.

"However, in spite of failures such as these, I am sure that the sense of responsible and indeed Christian partnership between the Church and the medical profession is increasing most healthily; and I think there are similar signs of renewed co-operation in other spheres of life also. Everything possible should be done by Churchmen and especially by the Church laity to stimulate and encourage hopeful developments."

Nuclear Energy in Medicine.—The Royal Marsden Hospital is to build a branch hospital at Sutton Downs devoted to the application of nuclear energy in medicine, and to research on the effects of radiation on man. It will be closely associated with the Institute of Cancer Research, the South Metropolitan Cancer Registry, and the Radiological Protection Service. The building programme has been planned in two stages, and it is hoped that work on the first, a treatment centre at which supervoltage radiotherapy will be available to a group of hospitals, will begin this summer and be completed in about two years' time. Advantage will be taken of a natural rise at the east end of the site to bury the supervoltage buildings in the side of the hill, using the chalky ground itself as a radiation shield instead of great thicknesses of concrete. The second stage, for which a detailed programme is not yet available, will be the erection of a radioactive isotopes investigation and treatment unit with research and teaching laboratories. Here, short-term courses in the use of radioactive isotopes in medicine will be arranged for home and overseas visitors. Accommodation is already available at Sutton Downs for the treatment of 12 patients by the first teletherapy unit using caesium 137 in Britain.

Rockefeller Foundation.—Rockefeller Foundation grants for the first quarter of the year totalled $2,296,466. Grants for medical education and public health accounted for $153,480, and biological and medical research for $780,366. Major grants were provided for research on population problems at Miami University (U.S.A.) and on tropical diseases at the Liberian Institute, Harbel, West Africa. In Britain a grant of $41,000 over a five-year period has been made for biochemical research into mental disease to be carried out at the University of Oxford under the general supervision of Sir GEORGE PICKERING, regius professor of medicine, to whose research the Foundation contributed $156,000 in 1955.

Engineering for Disabled.—The National Fund for Poliomyelitis Research has set up a committee for research into apparatus for the disabled under the chairmanship of Sir HARRY PLATT, emeritus professor of orthopaedic surgery at the University of Manchester. Its aim is "to tackle the problem of the disabled from a combined engineering and medical point of view." The National Fund has made a grant of £19,120 for an initial three-year period for this purpose, and has appointed a materials handling engineer at the Institute of Orthopaedics in London where prototypes will be made and research undertaken.

Polio Vaccine.—A temporary shortage of poliomyelitis vaccine, due to the increased demand for inoculation following the death of a well-known footballer from poliomyelitis, has now been overcome. The Ministry of Health announced this week that more than one million extra doses have been dispatched in the last 10 days to about 100 authorities, and that the United States is to supply about one million doses of vaccine to replenish the reserve stock.

Holiday Camp for the Handicapped.—The Gorleston Holiday Camp for the Handicapped, under the auspices of the Norfolk Association for the care of the Handicapped, will be run again this year from September 12 to 26, and will accommodate 300 guests a week. Application forms and brochures can be obtained from the Hon. Camp Secretary, N.A.C.H., 29, Thorpe Road, Norwich. Final applications must be returned by June 15.

Transport of Live Animals.—A British Standards Institution Committee under the chairmanship of Dr. W. LANE-PETTER has been formed to study the possibility of laying down British Standard recommendations for the carriage of live animals by air. The committee is giving priority to discussions on the transport of day-old chicks and of monkeys.

[Lanchester and Lodge, Architects

Model of Sutton Downs branch of Royal Marsden Hospital.

Joint B.M.A.-C.M.A. Annual Meeting.—Canadian cardiologists attending the Edinburgh meeting who would like to be put in touch with particular cardiac centres in this country should write to the Secretary, British Cardiac Society (Dr. P. Mounsey, 35, Flood Street, Chelsea, London, S.W.3), who will try to arrange for them to do so between July 8 and 17.

Central Midwives Board.—At a meeting of the Board last month Mr. ARNOLD WALKER was re-elected as chairman, and Professor A. A. MONCRIEFF as deputy chairman for the ensuing year.

COMING EVENTS

Fourth Almroth Wright Lecture.—"The Molecular Basis of Heredity," by Professor G. W. BEADLE. For details see advertisement p. 52 of this week's *Journal*.

National Deaf Children's Society.—The Society's Spring Meeting will be held at 2.30 p.m. on May 2 at the Holborn Borough Assembly Hall, John's Mews, Northington Street, London, W.C.1.

British Red Cross Society.—The society is holding an exhibition illustrating its work throughout the world at 14–15, Grosvenor Crescent, London, S.W.1, from May 4 to 8.

National Industrial Safety Conference and Trade Exhibition.—This will be held at Scarborough from May 8 to 10. Details from the Industrial Safety Division, Royal Society for the Prevention of Accidents, Artillery Mansions, 75, Victoria Street, London, S.W.1 (ABB 6963).

World Health Organization.—The twelfth World Health Assembly will be held in Geneva from May 12 for three weeks. Details from the W.H.O., Palais des Nations, Geneva, Switzerland.

London University Convocation.—Dr. C. F. HARRIS, vice-chancellor of the University, will address convocation on "Problems of Medical Education" on May 12 at 6 p.m. at the Senate House, Malet Street, London, W.C.1.

Joint Conference of the College of General Practitioners and the Society of Medical Officers of Health.—This conference will take place at the Wellcome Building, Euston Road, London, N.W.1, on May 23 and 24. Details from the secretary, the Society of Medical Officers of Health, Tavistock House South, Tavistock Square, London, W.C.1.

Institute for the Study and Treatment of Delinquency.—A week-end course for psychiatrists on "Assessing the Offender for the Courts" will be held at Moor Park College, Farnham, Surrey, from May 29 to 31. Details from Miss E. SAVILLE, I.S.T.D., 8, Bourdon Street, Davies Street, London, W.1. (MAY 3472.)

Eighth German Postgraduate Medical Congress.—This will be held in West Berlin from May 20 to 24. Details from Kongressgesellschaft für ärztliche Fortbildung e.V., Berlin-Steglitz, Klingsorstr. 21, Germany.

International Association of Gerontology.—The second meeting of the European Clinical Section will be held at Nancy and Vittel from June 25 to 28. Further details from Dr. E. WOODFORD-WILLIAMS, Department of Medicine and Geriatric Medicine, General Hospital, Sunderland.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, May 2

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Chest Clinic, Castle Hill, Cambridge. Symposium on Respiratory Diseases. 10.30 a.m., Dr. R. A. Bruce: Cough; 11.30 a.m., Mr. C. Parish: Haemoptysis; 12.15 p.m., Dr. E. M. Cheffins: Pain in the Chest; 2.15 p.m., Dr. M. J. Greenberg: Dyspnoea; 3 p.m., Mr B. B. Milstein: Dysphagia; 4 p.m., film: Treatment of Bronchiectasis, with commentary by Mr. P. R. Slade.

Monday, May 4

MARLBOROUGH DAY HOSPITAL.—8.15 p.m., Dr. S. L. Morrison: Epidemiology and Mental Illness.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Mr. Geoffrey Knight: Surgical Treatment of Mental Illness.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute of Microbiology 5 p.m., Almroth Wright Lecture by Professor P. B. Beeson (Yale): Studies on Bacterial Infections of the Kidney.

Tuesday, May 5

INSTITUTE OF DERMATOLOGY.—At British Institute of Radiology, 5 p.m., Dr. E. Wright: Effects of Irradiation on the Skin.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 2.30 p.m., Professor J. Walker: Oxygen Supply to the Human Foetus.

LIVERPOOL MEDICAL INSTITUTION.—5.15 p.m., joint history of medicine lecture by Dr. Robert Cope: Medicine in the early nineteenth century.

LONDON UNIVERSITY.—At Anatomy Lecture Theatre, University College, Gower Street, W.C., 5.30 p.m., special university lecture in human anatomy and morphology by Professor V. B. Mountcastle (U.S.A.): Central Nervous Mechanisms in Somatic Sensation—(1) Inter-relations of Structure and Function in the Somatic Afferent System.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. Desmond O'Neill: Tension Pain in Gynaecological Practice.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. J. Minton: Ocular Manifestations in Clinical Neurology. Part II.

WEST OF ENGLAND CHILD HEALTH GROUP.—At Department of Child Health Lecture Theatre, Children's Hospital, Bristol, 5.30 p.m., Dr. Cecile Hopkins: Problem Families.

Wednesday, May 6

ASSURANCE MEDICAL SOCIETY.—At Medical Society of London, 5 p.m., Dr. Francis Bach: Rheumatic Diseases and their Relation to Life Insurance.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Lymphocytic Infiltration of the Skin.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Sir Russell Brock: Present Position of the Surgery of Pulmonary Stenosis with Normal Aortic Root.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. I. Friedmann, Dr. D. A. Osborn, and Dr. A. L. Jeanes: Clinical pathological conference.

LONDON UNIVERSITY.—(1) At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in hygiene and public health by Professor Jonas E. Salk (Pittsburgh): Waxing and Waning of Epidemics in Our Time. (2) At Bedford College, N.W., 6 p.m., special university lecture in psychology by Professor D. J. van Lennep (Utrecht): Recent Studies on the Personality of the Proficient Research Worker.

MANCHESTER MEDICAL SOCIETY.—At Physiology Theatre. Manchester University Medical School, 5 p.m., annual meeting. Professor M. L. Rosenheim: A Medical Visit to the Antipodes.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. E. J. L. Lowbury: Infection of Burns.

Thursday, May 7

HONYMAN GILLESPIE LECTURE.—At Anatomy Theatre, University New Buildings, Edinburgh, 5 p.m., Professor H. N. Robson: Some Aspects of Leukaemia.

INSTITUTE OF NEUROLOGY.—5 p.m., Professor N. M. Dott: Syndromes of Cerebral Displacement.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—8.15 p.m., clinical meeting.

LONDON UNIVERSITY.—(1) At Anatomy Lecture Theatre, University College, Gower Street, W.C., 5.30 p.m., special university lecture in human anatomy and morphology by Professor V. B. Mountcastle (U.S.A.): Central Nervous Mechanisms in Somatic Sensation—(II) Neural Correlates of Tactile and Kinesthetic Sensibilities. (2) At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in microbiology by Dr. François Jacob (Paris): Viruses in Relationships with Some Genetic Elements of the Cell. (3) At Bedford College, N.W., 6 p.m., special university lecture in psychology by Professor D. J. van Lennep (Utrecht): Recent Studies on the Personality of the Proficient Research Worker.

NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Dr. J. Judet: Treatment of Talipes Equino-Varus in Children Beyond the Age of Two Years.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Raymond Daley: Mechanism and Treatment of Cor Pulmonale.

ROYAL EYE HOSPITAL.—5.30 p.m., Dr. T. H. Whittington: Aspects of Refraction Work—(6) Astigmatism.

ROYAL SOCIETY.—4.30 p.m., Croonian Lecture by Professor W. T. J. Morgan, F.R.S.: Contribution to Human Biochemical Genetics; Chemical Basis of Blood Group Specificity.

Friday, May 8

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 4.30 p.m., Third Knox Memorial Lecture by Dr. S. Cochrane Shanks: Medicine, Radiology, and the Law.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. P. D. Samman.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., clinical lecture by Mr. N. Asherson: Cysts of the Larynx and Pharynx.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. W. T. Irvine: Some Clinical and Experimental Problems of Ureteral Transplantation.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3.30 p.m., Professor J. B. Kinmonth: Some Aspects of Cardio-vascular Surgery.

WESTMINSTER HOSPITAL MEDICAL SCHOOL.—5.30 p.m., Clinico-pathological Conference: Aortic Coarctation.

Saturday, May 9

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, (1) 9.45 a.m., Professor H. Carey (New Zealand): Conservative Management of Toxaemia. (2) 11 a.m., Professor D. E. Cannell (Toronto): Management of Cardiac Diseases in Pregnancy.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bass.—On April 15, 1959, in University College Hospital, London, W.C., to Nesta (formerly Shiner), wife of Dr. A. L. Bass, a daughter—Gillian Anne.

Maling.—On April 21, 1959, in Swansea, to Rosemary (formerly Dearden), M.B., Ch.B., D.P.M., and Derek Hylton Maling, B.A., Ph.D., a daughter—Heather.

Moody.—On April 20, 1959, to Marion (formerly Lavers) and Dr. W. P. C. Moody, of 48, Chester Road, Northwood, Middx., a brother to Kingsley and Susan—Julian Christopher.

DEATHS

Blackmore.—On April 6, 1959, at 21, Lynwood Close, Woodham Lane, Woking, Surrey, Douglas William Nelson Blackmore, M.B., Ch.B., late of Thornton, Bradford, Yorks., aged 60.

Buckley.—On April 10, 1959, at St. Augustine's Home, Brighton, Sussex, Winifred Finnimore Buckley, O.B.E., M.R.C.S., L.R.C.P., formerly of 20, Lexham Gardens, London, W.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Poliomyelitis in Infancy

Q.—*Since poliomyelitis is said to be rare below the age of 1 year, and must be even rarer below the age of 3 months, is there any need to suspend injections of combined prophylactic during a poliomyelitis epidemic?*

A.—It is not correct to say that poliomyelitis is rare below the age of 1 year and even rarer below the age of 3 months. That no age is immune, in the sense that no age is exempt from contracting the disease, is an agreed fact: numerous cases below the age of 1 month and numerous cases above the age of 60 years have been observed. Recently the writer went over the figures of all *paralytic cases* of poliomyelitis admitted to one infectious diseases hospital during the previous 10 years. There were 314 cases, of which 22 (7%) were under 12 months, 12 under 6 months (2.3%), and 3 under 3 months (0.9%). McMath[1] has recorded recently a case of poliomyelitis with respiratory paralysis in an infant 26 days old, and has pointed out the large number of cases of paralytic poliomyelitis in infants which have been published. The incidence of poliomyelitis in infants is not negligible at present and it carries a heavy mortality (21 deaths in a series of 58).[2]

It must, however, be pointed out that a high proportion of newborn infants do have a passive immunity against all three types of poliomyelitis virus—62% according to Perkins, Yetts, and Gaisford.[3] This passive immunity is due to antibodies from the maternal blood and passes off between the 6th and 9th month. The apparent immunity which has been observed in infants is therefore limited to this group and is practically non-existent after the 9th month. It may well be that, with the present poliomyelitis vaccination campaign, the proportion of passively immune infants will be much higher in the next generation, but, until then, the risks of poliomyelitis in infants after combined prophylactics, especially the alum-containing ones, remain.

The actual number of cases of poliomyelitis in infants under 12 months after combined or alum-containing prophylactics given in the M.R.C. report[4] was 60, and under 6 months nil. But, as the authors of the report remarked, this is "largely a reflection of the small number of prophylactic inoculations given to children less than 6 months old."

REFERENCES

1 McMath, W. F. T., *Brit. med. J.*, 1959, 1, 98.
2 Bates, T., *Amer. J. Dis. Child.*, 1955, 90, 189.
3 Perkins, F. T., Yetts, R., and Gaisford, W., *Brit. med. J.*, 1958, 2, 68.
4 M.R.C. Report, *Lancet*, 1956, 2, 1223.

Sulphonamides in Pneumonia

Q.—*Have sulphonamides still a place in the treatment of pneumonia?*

A.—It is certainly reasonable to treat patients with pneumonia by means of sulphonamides. However, with the possibility of using phenoxymethyl penicillin by mouth, the sulphonamides have no longer this particular advantage. Also, if the infecting organism is a staphylococcus it will not be affected by the sulphonamides, whereas outside of hospitals it is very likely that penicillin will be effective against it. I think that on the whole the advantages of using penicillin are slightly greater than relying on the sulphonamides.

Inheritance of Myotonia Congenita

Q.—*A patient has two brothers affected with myotonia congenita. What is the likelihood of the patient having children similarly affected?*

A.—Myotonia congenita, or Thomsen's disease, is due in Dr. Thomsen's own family, in which there have now been 64 affected members, to a dominant mutant gene. In some other families, as in the patient's, only a pair of siblings were affected and the mode of inheritance is not clear.[1] No exact genetic prognosis can be given, but if the patient himself has no signs of myotonia congenita there is probably not a high risk of his children being affected.

REFERENCE

1 Thomasen, E., *Myotonia, Thomsen's Disease, Paramyotonia, Dystrophia Myotonica*, 1948. Copenhagen.

Sensitivity to Antihistamines

Q.—*Should mepyramine maleate be given by mouth to a patient who is sensitive to it when applied locally in a cream? Is there any substance in this group which it would be safe to give him?*

A.—It would certainly be risky to give mepyramine maleate by mouth to a patient who is sensitive to local application. Sensitivity to local application of antihistamine drugs is very common, and it is generally agreed that it is most unwise to use creams, etc., especially for any length of time. Oral administration is more effective for relieving itching skin conditions. Drugs similar in chemical structure to mepyramine maleate would be likely to cause sensitivity again in this patient. These are tripelennamine, methapyrilene, halopyramine, chlorpheniramine. Avoiding these, we still have a wide choice—for example, diphenylpyraline, chlorcyclizine, buclizine, triprolidine, etc.

NOTES AND COMMENTS

Ethyl Chloride, Nitrous Oxide, and Oxygen Mixture.—Dr. H. B. SANDIFORD (Southsea, Hants) writes: In the *Journal* of January 28, 1958 ("Any Questions?" p. 236) there was a question on apparatus for using ethyl chloride in an open circuit, particularly with a McKesson machine. The reply stated that there was no commercially available vaporizer to use ethyl chloride with the McKesson, Boyle, or Walton apparatus. This was not quite correct, as a reference was given to a very useful piece of apparatus designed by Dr. P. R. Bromage.[1] Some years ago I was given one of these by the McKesson Company and have used it with success ever since. One problem has been to get the necessary size of ethyl chloride container, but the British Oxygen Company has now made simple alterations to the original apparatus and any size of bottle can now be used. As stated in your answer to the original question, overdosage with ethyl chloride is a danger. If it is only given to a pink patient and in a dose of approximately 0.5 ml., which can be repeated, in my experience the risk is very small and the technique is useful from time to time, especially for dental extraction in young children.

REFERENCE

1 Bromage, P. R., *Anaesthesia*, 1950, 5, 94.

Correction.—In the letter on "Common Bile Duct after Cholecystectomy," from Mr. W. M. Capper and Mr. W. J. Gall (*Journal*, April 11, p. 973) "pre-operative" in the fourth line of the third paragraph should have read "per-operative." In the penultimate line of the letter the upper limit for the diameter of a normal duct should have been 10–11 mm. (*not* cm.).

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